Enclosure No:	**1/AWMSG/1117**
Agenda Item No:	**1** – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Minutes of the AWMSG meeting held Wednesday, 11th October 2017 commencing 9.30 am in 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 & Hospital Consultant	
2.	Professor John Watkins	Vice Chair & Consultant in Public Health Medicine	
3.	Dr Anwen Cope	Healthcare professional eligible to prescribe	
4.	Mr Stuart Davies	Finance Director	
5.	Mrs Ellen Lanham	Community Pharmacist	
6.	Prof Dyfrig Hughes	Health Economist	
7.	Dr Emma Mason	Clinical Pharmacologist	
8.	Mrs Alison Hughes	Managed Sector Primary Care Pharmacist	
9.	Mr Farhan Mughal	ABPI Cymru Wales	
10.	Mr Chris Palmer	Lay Member	
11.	Mr John Terry	Managed Sector Secondary Care Pharmacist	**1-10**
12.	Dr Jeremy Black	General Practitioner	

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

AWTTC Leads:
Ms Kath Haines, Head of WAPSU
Mr Richard Boldero, Senior Pharmacist
Dr Caron Jones, Senior Scientist
Dr Stephanie Francis, Senior Scientist
Mrs Sue Cervetto, Senior Pharmacist

Mrs Sabrina Rind, Senior Pharmacist
Dr David Jarrom, Senior Scientist
Ms Kelly Wood

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
EMIG	Ethical Medicines Industry Group
EOL	End of life
FAR	Final Appraisal Recommendation
FDA	US Food and Drug Administration
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health 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
PAMS	Patient Access to Medicines Service
PAR	Preliminary Appraisal Recommendation
PAS	Patient Access Scheme
PPRS	Prescription Price Regulation Scheme
SMC	Scottish Medicines Consortium
SPC	Summary of Product Characteristics
TDAPG	Therapeutic Development Appraisal Partnership Group
T&FG	Task and Finish Group
UHB	University Health Board
WAPSU	Welsh Analytical Prescribing Support Unit
WCPPE	Welsh Centre for Pharmacy Postgraduate Education
WeMeReC	Welsh Medicines Resource Centre
WG	Welsh Government
WHO	World Health Organization
WHSSC	Welsh Health Specialised Services Committee
WPAS	Wales Patient Access Scheme

1. Welcome and introduction

The Chairman welcomed members. He confirmed that the morning session would be conducted in private to maintain commercial confidentiality; thereafter, the meeting would be opened to the public.

2. Apologies

Dr Sian Lewis and Dr Pushpinder Mangat, Welsh Health Specialised Services Committee
Dr Cath Bale and Dr Sue Jeffs, Hospital Consultant
Dr Mark Walker, Medical Director
Mrs Louise Williams, Senior Nurse

3. Declarations of interest

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

4. Minutes of previous meeting

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

5. Appraisal 1: Full Submission

Lenvatinib (Lenvima®) for the treatment of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine (RAI)

The Chairman welcomed delegates from Eisai Pharmaceuticals Ltd.

The Chair sought confirmation that members had access to the AWMSG policy for appraising orphan, ultra-orphan medicines and medicines developed specifically for rare diseases.

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 explained that NMG had considered the clinical and cost-effectiveness issues in detail and had also taken account of clinical expert and patient views. He informed members there was no requirement to repeat this discussion. The Chairman asked members to highlight any outstanding clinical or cost-effectiveness issues and consider the company response to the preliminary recommendation. He explained that AWMSG would focus on the budget impact and wider societal issues.

Dr Stephanie Francis, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR.

Dr Al-Ismail confirmed that NMG had appraised Lenvatinib (Lenvima®) on 6th September 2017 and recommended use as an option within NHS Wales for the treatment of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine (RAI). He relayed the view of NMG that the recommendation should apply only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price. Dr Al-Ismail confirmed that NMG were of the view that the criteria for appraisal of this medicine via AWMSG's process for appraising orphan, ultra-orphan and medicines developed specifically for rare medicines had been met; however, the policy for appraising medicines at end of life could not be applied as the median survival was more than twenty-four months.

Dr Francis relayed the view of clinical expert. They highlighted that there was an unmet need and that best supportive care is the most appropriate comparator as sorafenib is not routinely available for patients in Wales. Clinical experts confirmed that the number of eligible patients is

likely to be small as many patients cannot tolerate the treatment. Dr Francis informed members that clinical experts had raised the issue of inequity in access as patients in Wales have no treatment options for thyroid carcinoma that is refractory to radioactive iodine. It was confirmed that NMG were satisfied that the company's approach regarding median treatment duration and median dose was reasonable. Dr Francis highlighted that clinical guidelines support use of a tyrosine kinase inhibitor in radioactive iodine refractory thyroid cancer.

The Chairman opened discussion in relation to clinical effectiveness and members sought clarification in relation to treatment dosing. Dr Francis highlighted that the clinical expert has suggested that very few patients would received the licensed 24 mg dose due to toxicity and adverse events. Members explored the availability of outcome evidence in relation to a reduced dose and the company delegates informed members of the compassionate use programme in England. There was discussion over the study end-points and members sought clarification regarding the overall survival data. Delegates informed the committee that the cross-over design of the study will cause an underestimation of the efficacy of lenvatinib compared to placebo. The company delegates confirmed that quality of life evidence would be available in three to four years, and acknowledged there is limited clinical experience currently in the UK.

The Chairman invited Professor Dyfrig Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed that he took no part in the production of the ASAR and was in attendance as the voting health economist member of AWMSG. He summarised the evidence presented in the case for cost-effectiveness and highlighted the uncertainties in the modelling. The key issues outlined in the ASAR were highlighted. Professor Hughes commented on the budget impact estimates and informed members that the budget impact had been based on 11 eligible patients in year 1-5 with an estimated uptake of 10% in year 1, rising to 50% in year 5. The company delegates accepted the overview provided to members and had no additional comments. The Chair reminded members that in line with AWMSG's policy for appraising orphan and ultra-orphan medicines members could apply a degree of latitude in relation to the cost per QALY. The company delegates were asked to comment on the non-UK data and explain the process for data collection and validation.

The Chairman referred members to the two patient organisation questionnaires submitted by the Butterfly Thyroid Cancer Trust and the British Thyroid Foundation and asked the lay member, Mr Chris Palmer, to relay the key points. Mr Palmer stated that the medicine offered hope to patients where normal treatment had failed and highlighted the positive impact this had on patients and their families. Treatment enabled patients to have more normality in their day to day life, with fewer hospital visits and increased quality time at home. It was the view of patients that the advantages offered by the treatment outweighed the disadvantages of the side effects. The Chairman was encouraged by the level of response from patients. There we no other wider society issues of note.

The Chairman referred to the response from Eisai Ltd to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. The delegates thanked AWMSG for the opportunity to input into the discussion and respond to questions. In concluding, the Chairman thanked the company delegates and, 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:

Lenvatinib (Lenvima®) is recommended as an option for use within NHS Wales for the treatment of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine

(RAI). This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

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

7. Appraisal 2: Full Submission

Glecaprevir/pibrentasvir (Maviret®) for the treatment of chronic hepatitis C virus infection in adults

The Chairman welcomed delegates from AbbVie 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 explained that NMG had considered the clinical and cost-effectiveness issues in detail and had also taken account of clinical expert and patient views. He informed members there was no requirement to repeat this discussion. The Chairman asked members to highlight any outstanding clinical or cost-effectiveness issues and consider the company response to the preliminary recommendation. He explained that AWMSG would focus on the budget impact and wider societal issues.

The Chairman informed the company delegates that they would be asked to leave the meeting for a short period at the appropriate time to enable AWMSG to have a confidential discussion, as the comparator medicine also had an associated patient access scheme.

Dr David Jarrom, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR. Members were informed that clinicians in Wales had sought early AWMSG advice ahead of the NICE appraisal determination, which is expected to be published in March 2018. Dr Jarrom provided a comprehensive summary of the evidence, clarified the licensed indication and relayed the views of the clinical experts.

Dr Al-Ismail confirmed that NMG had appraised glecaprevir/pibrentasvir (Maviret®) on 6th September 2017 and recommended use as an option within NHS Wales for the treatment of chronic hepatitis C virus (HCV) infection in adults. He relayed the view of NMG that the recommendation should apply only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

The Chairman opened the discussion in relation to clinical effectiveness. Reference was made to the All-Wales Hepatitis C roll out programme guidelines, which recommend treatments for hepatitis C based on evidence and cost. Clarification was sought in relation to the licence and patient population. There was discussion over the number of eligible patients in Wales. The Chair referred to the clinical expert summary. Experts stated that as some treatments are not suitable for some patients, and as some treatments also fail to clear the virus in some patients, a choice of treatments was welcomed.

The Chairman invited Professor Dyfrig Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed that he took no part in the production of the ASAR and was in attendance as the voting health economist member of AWMSG. He summarised the evidence presented in the case for cost-effectiveness and highlighted the potential financial savings to NHS Wales which were based on the acquisition cost with the utilisation of the Wales Patient Access Scheme. Delegates from AbbVie Ltd briefly left the meeting while the budget impact of the medication was considered in comparison to the competitor's PAS pricing.

The Chairman referred members to the patient organisation questionnaires submitted by the Hepatitis C Trust. Mr Palmer relayed the view that the most significant advantage of glecaprevir/pibrentasvir is its potential to widen access to interferon-free treatments to people who are not currently able to access such treatment (such as those with genotype 2 hepatitis C). It was noted that post-treatment times are significantly improved compared to interferon-based treatments and this enables individuals to resume normal family and working life as quickly as possible with minimal side-effects. The patient organisation highlighted that the medicine has demonstrated high cure rates in clinical trials and has the potential to halt damage to the liver, as well as eliminate the non-liver health impact of hepatitis C, which can be substantial. Mr Palmer informed members that the medicine is easy to administer and treatment is convenient for patients, both of which positively impact on adherence. The advantages of having treatment options available to patients and clinicians, as well as market competition, were noted.

The Chairman referred to the response from AbbVie Ltd to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. The company delegates thanked AWMSG for the opportunity to participate in the discussion. They highlighted the benefits of the treatment and encouraged a positive recommendation to help eliminate HCV. In concluding, the Chairman thanked the company delegates and, 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. Members retired to vote in private.

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:

Glecaprevir/pibrentasvir (Maviret®) is recommended as an option for use within NHS Wales for the treatment of chronic hepatitis C virus (HCV) infection in adults. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

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

8. Appraisal 3: Limited Submission
Dolutegravir (Tivicay®) in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) infected children aged 6–12 years

The Chairman welcomed delegates from ViiV Healthcare UK 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 informed members that the application had been considered eligible for a limited submission and no cost-effectiveness information is required. He confirmed that for a limited submission 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 the right to request a full submission if the budget impact exceeded that estimated in the submission.

Dr Caron Jones, the AWTTC Appraisal Lead, set the context of the appraisal of dolutegravir (Tivicay®) as a minor licence extension in paediatric patients and relayed the key aspects of the submission outlined in the ASAR. Dr Jones highlighted that a Wales Patient Access Scheme had been approved and budget impact based on two patients in Wales would vary depending on the weight of the child.

Dr Al-Ismail confirmed that NMG had appraised dolutegravir (Tivicay®) on 6th September 2017 and recommended use as an option within NHS Wales in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) infected adults, adolescents and children above 6 years of age. It was noted that the recommendation would apply only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

The Chairman invited comment on the case for clinical effectiveness. Clarification was sought in relation to granule and suspension formulations. It was noted that the applicant company estimated there were seven children who may be eligible for treatment. The view of clinical experts was that four children may be eligible for treatment. It was noted that a once daily treatment may offer a benefit in terms of adherence.

The Chairman confirmed that no patient organisation questionnaires had been submitted and Mr Palmer informed members of the organisations that had been approached by AWTTC. Mr Palmer welcomed wider access and more choice for clinicians and patients.

The Chairman referred to the response from ViiV Healthcare UK Ltd to the preliminary recommendation and asked the delegate if she wished to make any closing remarks. In concluding, the Chairman thanked the company delegates and, 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. Members retired to vote in private.

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:

Dolutegravir (Tivicay®) is recommended as an option for use within NHS Wales in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) infected adults, adolescents and children above 6 years of age.

This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

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

8. Appraisal 4: Full Submission

C1 inhibitor (human) (Cinryze®) for the treatment and pre-procedure prevention of angioedema attacks in children aged 2–11 years with hereditary angioedema (HAE); routine prevention of angioedema attacks in children aged 6–11 years with severe and recurrent attacks of HAE, who are intolerant to or insufficiently protected by oral prevention treatments, or patients who are inadequately managed with repeated acute treatment

The Chairman welcomed delegates from Shire 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 informed members that the application had been considered eligible for a limited submission and no cost-effectiveness information is required. He confirmed that for a limited submission 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 the right to request a full submission if the budget impact exceeded that estimated in the submission.

The Chairman sought clarification that all members had access to AWMSG's policy for appraising orphan, ultra-orphan medicines and medicines developed specifically for rare diseases. The Chairman informed the company delegates that they would be asked to leave the meeting for a short period at the appropriate time to enable AWMSG to have a confidential discussion, as the comparator medicine had a Welsh Patient Access Scheme.

Ms Kelly Wood, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR. Ms Wood highlighted that AWMSG had previously recommended this medicine for use in adults and adolescents, and a limited submission had been considered acceptable as it was a minor licence extension for use in children. Ms Wood asked members to note that the company had used Berinert® as a comparator to inform their budget impact model. There is no direct comparative data with Berinert® and the company considered an indirect comparison unfeasible due to low patient numbers. Ms Wood informed members that clinical experts in Wales had confirmed that Berinert® is the only alternative to Cinryze® in Wales at present. Cinryze® was highlighted as the only non-oral preparation licensed for the routine prevention of angioedema attacks in paediatric patients. Members were informed that the total number of patients eligible for treatment with Cinryze® in Wales is 62 and that consideration is also required to the AWMSG policy for appraising orphan and ultra-orphan and medicines developed specifically for rare diseases.

Dr Al-Ismail confirmed that NMG had appraised C1 inhibitor (human) (Cinryze®) on 6th September 2017 and recommended use as an option within NHS Wales for the treatment and pre-procedure prevention of angioedema attacks in adults, adolescents and children (2 years old and above) with hereditary angioedema (HAE); routine prevention of angioedema attacks in adults,

adolescents and children (6 years old and above) with severe and recurrent attacks of HAE, who are intolerant to or insufficiently protected by oral prevention treatments, or patients who are inadequately managed with repeated acute treatment. Dr Al-Ismail stated that NMG were satisfied that the AWMSG criteria for a medicine developed specifically for rare diseases had been met. NMG were of the view that therapy should be initiated under the supervision of a physician experienced in the care of patients with hereditary angioedema. NMG recommended that the medicine should be prescribed by brand name to avoid automatic substitution and therefore help with pharmacovigilance.

The Chairman opened the discussion in relation to clinical effectiveness. It was noted that there is no non-IV treatment option available currently and very few patients would be suitable for routine access to the medicine. There were no outstanding clinical issues of note. Ms Wood confirmed that Cinryze® offers a simple non-weight based dosing across all indications in paediatric patients. It was noted that the licensed indication covers an area where there is no other licensed treatment for the routine prevention of angioedema attacks in paediatric patients. Clarification was sought in relation to patient numbers and Ms Wood confirmed that experts estimated 5 eligible patients in Wales would be eligible for the treatment and pre-procedure prevention of hereditary angioedema attacks. The company delegates left the room and the Chairman referred members to the budget impact estimates. There were no outstanding issues of note. Mr Palmer confirmed that seven patient organisations had been approached and invited to submit views, but none had done so.

The Chairman referred to the response from Shire Pharmaceuticals Ltd to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. In concluding, the Chairman thanked the company delegates and, 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. Members retired to vote in private.

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:

C1 inhibitor (human) (Cinryze®) is recommended as an option for use within NHS Wales for the treatment and pre-procedure prevention of angioedema attacks in adults, adolescents and children (2 years old and above) with hereditary angioedema (HAE); routine prevention of angioedema attacks in adults, adolescents and children (6 years old and above) with severe and recurrent attacks of HAE, who are intolerant to or insufficiently protected by oral prevention treatments, or patients who are inadequately managed with repeated acute treatment.

This advice incorporates and replaces the existing AWMSG recommendation on C1 inhibitor (Cinryze®) for the treatment and pre-procedure prevention of angioedema attacks in adults and adolescents with HAE, and routine prevention of angioedema attacks in adults and adolescents with severe and recurrent attacks of HAE who are intolerant to or insufficiently protected by oral prevention treatments or who are inadequately managed with repeated acute treatment (Advice number 0313, originally published March 2013). The Chairman announced that confirmation of AWMSG's recommendations would be forwarded within five working days to the applicant company who have up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

9. Chairman's report

The Chairman confirmed Welsh Government ratification of AWMSG's advice in relation to Ivacaftor (Kalydeco®) which was recommended for restricted use within NHS Wales for the treatment of patients with cystic fibrosis (CF) aged 18 years and older who have an *R117H*

mutation in the CF transmembrane conductance regulator (*CFTR*) gene. He informed members that AWTTC were in the process of informing the Service and updating the website.

The Chairman reported that Clinuval Pharmaceutial Limited had submitted a request for independent review of AWMSG's recommendation announced on 13th September 2017 in relation to afamelanotide (Scenesse) for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria. The medicine had not been supported by the committee for use within NHS Wales. The Chairman confirmed the appraisal process had been suspended pending investigation of the grounds for this request.

The Chairman announced forthcoming consultations and invited comment on:

- National Prescribing Indicators 2018–2019
- Safe Use of Proton Pump Inhibitors
- All Wales Guide: Pharmacotherapy for Smoking Cessation
- AWMSG's Medicines Strategy 2018-2023

The Chairman announced an AWMSG Masterclass would be held in Cardiff on 22nd November 2017 and encouraged the pharmaceutical industry to attend and learn about the work of AWMSG and how to get the best outcome from AWMSG's health technology appraisal process.

The Chairman announced an AWMSG training day for member and deputies of AWMSG, NMG and AWPAG would be held on 17th January 2018 in Cardiff City Stadium.

The Chairman reminded members that all appraisal questioning should fall within the appropriate scope and parameters for AWMSG decision-making, and should only relate to the licensed indication. The Chairman asked members to make recommendations based on the evidence provided and following full and open discussion at the meeting today.

The Chairman announced the appraisals scheduled for the next AWMSG meeting to be held on 8th November 2017 in Cardiff:

Pegvisomant (Somavert) for the treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalize IGF-I concentrations or was not tolerated
Applicant Company: Pfizer Ltd

Stiripentol (Diacomit) in conjunction with clobazam and valproate as adjunctive therapy of refractory generalized tonic-clonic seizures in patients with severe myoclonic epilepsy in infancy (SMEI, Dravet's syndrome) whose seizures are not adequately controlled with clobazam and valproate
Applicant Company: Biocodex

Levodopa-carbidopa intestinal gel (Duodopa) for the treatment of advanced levodopa-responsive Parkinson's disease with severe motor fluctuations and hyper-/dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results
Applicant Company: AbbVie Ltd

The Chairman asked members to contact AWTTC ahead of the next meeting if they had any personal or non-personal interests to declare. Patients, patient organisations and patient carers were invited to submit their views on the medicines to be appraised via the AWMSG website or by contacting Ruth Lang at AWTTC for further information on the appraisal process and future work programme.

Mr John Terry Joined the meeting.

10. Appraisal 5: Full Submission

5-aminolevulinic acid (Ameluz®) for the treatment of superficial and/or nodular basal cell carcinoma unsuitable for surgical treatment due to possible treatment-related morbidity and/or poor cosmetic outcome in adults

The Chairman welcomed representation from the marketing authorisation holder, Biofrontera.

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 explained that NMG had considered the clinical and cost-effectiveness issues in detail and had also taken account of clinical expert and patient views. He informed members there was no requirement to repeat this discussion. The Chairman asked members to highlight any outstanding clinical or cost-effectiveness issues and consider the company response to the preliminary recommendation. He explained that AWMSG would focus on the budget impact and wider societal issues.

Mrs Sue Cervetto, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR. Mrs Cervetto highlighted that a positive AWMSG recommendation had previously been issued for the treatment of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2) and of field cancerization in adults. It was noted that SMC had issued negative advice for the indication being appraised by AWMSG, but a resubmission by the Biofrontera is back on the SMC work programme.

Dr Al-Ismail confirmed that NMG had appraised 5-aminolaevulinic acid (Ameluz®) on 6th September and recommended its use as an option within NHS Wales for the treatment of superficial and/or nodular basal cell carcinoma unsuitable for surgical treatment due to possible treatment-related morbidity and/or poor cosmetic outcome in adults.

The Chairman invited comment in relation to the case for clinical-effectiveness. There were no outstanding issues of note. Mrs Cervetto relayed that Ameluz® is administered in exactly the same way, and has a similar adverse reaction profile to Metvix®; the comparator provided in the evidence submitted. She confirmed the view of the clinical expert who had attended NMG that the trial evidence fits in with clinical practice in Wales. Clarification was sought in relation to the number of tubes used in treatment and storage. The company delegate highlighted that Ameluz® penetrates deeper into the skin and that evidence is available to demonstrate superiority. There was no unmet need identified in NHS Wales.

The Chairman invited Professor Dyfrig Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed that he took no part in the production of the ASAR and was in attendance as the voting health economist member of AWMSG. He summarised the evidence presented in the case for cost-effectiveness and highlighted the limitations of the economic analysis. It was noted that the CMA had been based on non-inferiority. The applicant company reported no significant differences in the safety of Ameluz® and Metvix®. Professor Hughes commented on the budget impact estimates which had been based on incidence rates. It was noted that many inputs could not be verified by AWTTC. A modest cost saving was noted, with the specific degree of saving dependent on the number of treatment tubes required.

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

The Chairman referred to the response from Biofrontera to the preliminary recommendation and asked the delegate for any 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:

5-aminolaevulinic acid (Ameluz®) is recommended as an option for use within NHS Wales for the treatment of superficial and/or nodular basal cell carcinoma unsuitable for surgical treatment due to possible treatment-related morbidity and/or poor cosmetic outcome in adults.

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

11. Appraisal 6: Full Submission
Tiotropium (Spiriva® Respimat®) as an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥800 µg budesonide/day or equivalent) and long-acting β2 agonists and who experienced one or more severe exacerbations in the previous year

The Chairman welcomed delegates from Boehringer Ingelheim 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 explained that NMG had considered the clinical and cost-effectiveness issues in detail and had also taken account of clinical expert and patient views. He informed members there was no requirement to repeat this discussion. The Chairman asked members to highlight any outstanding clinical or cost-effectiveness issues and consider the company response to the preliminary recommendation. He explained that AWMSG would focus on the budget impact and wider societal issues.

Mrs Sabrina Rind, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR. Mrs Rind highlighted that the medicine had been appraised in 2015 and had not been recommended for use in NHS Wales. Mrs Rind confirmed that tiotropium is the first long acting muscarinic antagonist for use as an add-on maintenance bronchodilator in asthma that works by opening the airways by relaxing the muscles that surround them. She highlighted strong clinical expert support for the medicine, and that it is included in the British Thoracic Society/Scottish Intercollegiate Network (BTS/SIGN) guidelines and is available in NHS England and Scotland. Mrs Rind confirmed that the resubmission was

based on a revised list price and an update to the BTS/SIGN guidelines.

Dr Al-Ismail confirmed that NMG had appraised tiotropium (Spiriva® Respimat®) on 6th September and recommended use as an option for treatment as an add-on maintenance bronchodilator in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥800 µg budesonide/day or equivalent) and long-acting β2 agonists and who experienced one or more severe exacerbations in the previous year.

The Chairman invited comment in relation to the case for clinical effectiveness. Dr Al-Ismail highlighted national support by clinicians in Wales for this medicine and highlighted the inequity in access. Clinicians had highlighted an unmet need and stated it would be a useful add-on for difficult to treat asthma. Members were informed that the clinical expert who had attended NMG had stated that it was particularly difficult to treat this patient group and clinicians had extensive experience in using tiotropium for a different indication. It was stated that anecdotal feedback reported an improved quality of life for patients. The clinical expert stated that this group of patients would be under specialist care and they anticipated that tiotropium would only be prescribed by a specialist. There was discussion over the trial data results. The absence of a comparator was noted and the company provided their rational for using best supportive care and highlighted the lack of evidence for other treatment options used at the same stage in treatment.

The Chairman invited Professor Dyfrig Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed that he took no part in the production of the ASAR and was in attendance as the voting health economist member of AWMSG. He summarised the evidence presented in the case for cost-effectiveness. It was noted that the model was well structured. There were no other issues of note.

The Chairman confirmed that no patient organisation questionnaires had been submitted. Mr Palmer informed members of the two organisations that had been contacted by AWTTC. Mr Palmer highlighted the potential to reduce the number of work days lost due to exacerbation and welcomed equity of access for patients. The ease of use and effective delivery of the inhaler was noted.

The Chairman referred to the response from Boehringer Ingelheim Ltd to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. In concluding, the Chairman thanked the company delegates and, 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. Members retired to vote in private.

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

12. Medicines Identified as Low Priority Funding in NHS Wales

The Chairman invited Mr Jonathan Simms, Clinical Director of Pharmacy at Aneurin Bevan UHB to present Enc 8 – Medicines Identified as Low Priority for Funding in NHS Wales.

The Chairman provided the background and confirmed that opportunity had been extended to members at the previous meeting held in September to comment on this paper. Subsequent to the meeting, members had provided further feedback and the paper had been updated by the author taking into account the comments received and was being re-presented to AWMSG for endorsement.

Mrs Samuels confirmed that AWTTC had acted upon the suggestion put forward at the previous meeting to include the development of a process to support the appropriate disinvestment of medicines of limited efficacy in NHS Wales within the new AWMSG Medicines Strategy 2018 to 2023. There was agreement that advising Welsh Government and NHS Wales on how health boards and other relevant organisations might implement the advice and strategy within the financial constraints placed upon them was within the remit of AWMSG. Mrs Samuels confirmed that AWTTC would relay the views of AWMSG to Welsh Government officials that the validation of evidence by AWTTC and full consultation would need to be an integral part of this process.

Mr Simms explained the purpose of the document and highlighted that Welsh Government, NHS Wales Chairs, Chief Executives and Medical Directors had agreed a National Improvement Programme which includes a commitment to identify opportunities to improve primary care prescribing and develop a list of medicines for restricted use. Members were informed that this work has been progressed via the Pharmacy Directors Peer Group and was based on priority areas identified by NHS Clinical Commissioners. He explained that the paper aimed to reduce inappropriate variation in prescribing of medicines identified as low priority for funding across NHS Wales to ensure health boards and clinicians are able to make the most efficient use of the resources available to them. Mr Simms presented the proposals to minimise the prescribing of medicines that offer a limited clinical benefit to patients and where more cost effective treatments may be available. He informed members that the document has been endorsed by NHS Wales Chief Executives and Medical Directors.

The Chairman invited Ms Kath Haines to comment. Ms Haines confirmed the standing of PresQIPP within NHS England and drew member's attention to the process for quality assurance.

The Chairman opened the discussion. There was broad support of the proposals; members asked for an assurance that a review of the evidence had been undertaken by AWTTC. There was discussion over the change of the wording 'should not be prescribed' to 'should not be routinely prescribed'. Mr Simms confirmed that the wording was consistent with NHS England. It was noted that co-proxamol should not be prescribed within NHS Wales. A suggestion was made that education to support these proposals could include a WeMeReC bulletin and other educational tools were suggested. The Chairman concluded the discussion by confirming AWMSG's endorsement of the paper.

The Chairman confirmed the date of the next meeting and closed the meeting.

Date of next meeting – Wednesday, 8th November 2017 in Cardiff.