Enclosure No:	**1/AWMSG/0918**
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, 18th July 2018 commencing 9.30 am at the Copthorne Hotel, Copthorne Way Culverhouse Cross, Cardiff, CF5 6DH

VOTING MEMBERS PRESENT:			**Did not participate in**
1.	Dr Stuart Linton	Chair & Hospital Consultant	
2.	Dr Jeremy Black	General Practitioner	
3.	Dr Anwen Cope	Other professions eligible to prescribe	
4.	Mr Stuart Davies	Finance Director	
5.	Prof Dyfrig Hughes	Health Economist	
6.	Dr Emma Mason	Clinical Pharmacologist	
7.	Mr Rob Thomas	ABPI Cymru Wales	
8.	Mr Chris Palmer	Lay Member	
9.	Dr Mark Walker	Medical Director	
10.	Prof John Watkins	Public Health Wales (AWMSG Vice Chair)	
11.	Mr Roger Williams	Managed Sector Secondary Care Pharmacist	9-11

IN ATTENDANCE:
Dr James Coulson, NMG Chair
Mrs Karen Samuels, Head of PAMS, AWTTC
Mrs Ruth Lang, Senior Liaison Manager, AWTTC

AWTTC Leads:
Ms Kath Haines, Head of WAPSU
Mrs Sabrina Rind, Senior Pharmacist
Dr Caron Jones, Senior Scientist
Dr Stuart Keeping, Senior Scientist

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
ASAR	AWMSG Secretariat Assessment Report
AWMSG	All Wales Medicines Strategy Group
AWPAG	All Wales Prescribing Advisory Group
AWTTC	All Wales Therapeutics & Toxicology Centre
BMA	British Medical Association
CAPIG	Clinical and Patient Involvement Group
CEPP	Clinical Effectiveness Prescribing Programme
CHMP	Committee for Medicinal Products for Human Use
DoH	Department of Health
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 Board
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
NPI	National Prescribing Indicator
PAMS	Patient Access to Medicines Service
PAR	Preliminary Appraisal Recommendation
PAS	Patient Access Scheme
PPRS	Prescription Price Regulation Scheme
SMC	Scottish Medicines Consortium
SPC	Summary of Product Characteristics
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 Chair opened the meeting and welcomed members.

2. Apologies

Dr Cath Bale, Hospital Consultant
Prof Iolo Doull and Dr Sian Lewis, WHSSC
Mr Stefan Fec, Community Pharmacist
Mrs Alison Hughes, Managed Sector Primary Care Pharmacist
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.

Before opening up the appraisal session the Chair 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. It was confirmed that the first appraisal would be conducted in private to protect commercial confidentiality as this submission had an associated Wales Patient Access Scheme (WPAS)

5. Appraisal 1: Full Submission (WPAS)

Telotristat ethyl (Xermelo®) for the treatment of carcinoid syndrome diarrhoea in combination with somatostatin analogue (SSA) therapy in adults inadequately controlled by SSA therapy

The Chair welcomed delegates from Ispen Ltd and it was confirmed that individuals in the public gallery were affiliated staff to AWTTC or Welsh Government.

The Chair invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chair announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on health boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published.

Dr Caron Jones, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the resubmission as outlined in the ASAR. It was noted that the marketing authorisation holder had proposed a restriction within its licensed indication for the treatment of carcinoid syndrome diarrhoea in adults who are inadequately controlled by somatostatin analogue (SSA) therapy and who experience an average of four or more bowel movements a day. Dr Jones confirmed that telotristat ethyl is the only licensed medicine for this condition. It was noted that SMC had accepted the medicine for restricted use in Scotland.

The Chair invited the NMG Chair, Dr James Coulson, to relay relevant issues from the appraisal by NMG held on 13th June. Dr Coulson confirmed that based on evidence of clinical effectiveness and cost-effectiveness, and having taken the views of clinicians and patients into account, NMG had supported use of telotristat ethyl (Xermelo®) within NHS Wales for restricted use within the indication being appraised by AWMSG. It was confirmed that NMG considered the criteria for appraisal under AWMSG's orphan/ultra-orphan/rare medicine policy had been met.

The Chair referred member to this policy for appraising orphan and ultra-orphan medicines, and medicines developed specifically for rare medicines which had been tabled. The Chairman opened discussion in relation to clinical effectiveness. There was discussion in relation to high placebo response rates and differences in absorption rates. The company delegates acknowledged the small numbers in the study and confirmed that all were in the restricted patient population. Members discussed response rates and treatment duration. It was noted that if no clinical benefit was derived within twelve weeks treatment would stop. Members considered the safety profile and the company delegates were asked to provide clarification of potential adverse reactions. Dr Jones confirmed that the clinical expert had recognised that there was an unmet

need to treat carcinoid syndrome diarrhoea. The drive to improve quality of life for patients in Wales was also noted.

Professor Dyfrig Hughes confirmed his role as AWMSG health economist and confirmed that he took no part in the production of the ASAR. He provided an overview of the case for cost-effectiveness as outlined in the ASAR and the company delegates acknowledged it to be a fair summary. Professor Hughes highlighted the limitations of the evidence. The company delegates agreed there were uncertainties and it had been difficult to make the case for cost-effectiveness due to the paucity of the data. Clarification was sought in relation to the utility values.

Dr Chris Palmer, relayed the key issues as outlined in the patient organisation submissions from NET Patient Foundation and an individual patient. Mr Palmer reiterated the importance of being able to do normal day to day routine activities such as walking the dog or shopping – activities that would be difficult to do given the unpredictability of the symptoms. Mr Palmer made the point that access to SSA therapy across Wales was variable - the Chair confirmed this was outside the scope of the appraisal. Mr Palmer reiterated the importance of having a licensed treatment available to patients and asked members to allow some latitude given that this was an orphan medicine. There were no other societal issues of note.

The Chair referred to the response from Ipsen 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 acknowledge it to be a fair and balanced appraisal. The Chairman thanked all delegates for a full and helpful discussion.

Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chair closed the appraisal.

Appraisal decision subsequently announced in public:
The Chair confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Telotristat ethyl (Xermelo®) is recommended as an option for restricted use within NHS Wales. Telotristat ethyl (Xermelo®) is licensed for the treatment of carcinoid syndrome diarrhoea in combination with somatostatin analogue (SSA) therapy in adults inadequately controlled by SSA therapy. Telotristat ethyl (Xermelo®) is restricted for use for the treatment of carcinoid syndrome diarrhoea in adults who are inadequately controlled by SSA therapy and who experience an average of four or more bowel movements a day. Telotristat ethyl (Xermelo®) is not recommended for use within NHS Wales outside of this subpopulation. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

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

The meeting was opened to the public.

6.

Chairman's report (verbal update)
It was reported that Welsh Government had ratified AWMSG's advice announced in May:

Icatibant acetate (Firazyr®) is recommended as an option for use within NHS Wales for the symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults, adolescents and children aged 2 years and older, with C1-esterase-inhibitor deficiency.
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.

Ranibizumab (Lucentis®) is recommended as an option for use within NHS Wales for the treatment of visual impairment in adults due to choroidal neovascularisation not due to pathological myopia or wet age-related macular degeneration.
This recommendation applies only in circumstances where the approved Patient Access Scheme (PAS) is utilised or where the list/contract price is equivalent or lower than the PAS price.

Selexipag (Uptravi®) is recommended as an option for restricted use within NHS Wales.
Selexipag (Uptravi®) is licensed for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients with WHO functional class (FC) II–III, either as combination therapy in patients insufficiently controlled with an endothelin receptor antagonist (ERA) and/or a phosphodiesterase type 5 (PDE-5) inhibitor, or as monotherapy in patients who are not candidates for these therapies. Selexipag (Uptravi®) is recommended as an option for restricted use within NHS Wales as a triple combination therapy for the treatment of pulmonary arterial hypertension (PAH) in adult patients with WHO functional class (FC) III who are insufficiently controlled on dual therapy with an endothelin receptor antagonist and a phosphodiesterase type 5 inhibitor. Selexipag (Uptravi®) is not recommended for use within NHS Wales outside of this sub-population.
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.

Members were informed that the applicant companies had been informed and the advice published on the AWMSG website.

It was reported that in the absence of a submission from the holders of the marketing authorisation, one Statement of Advice had been ratified by Welsh Government and published on the AWMSG website:

Nilotinib (Tasigna®) [AWTTC ref: 3615] for the treatment of paediatric patients with newly diagnosed Philadelphia chromosome positive chronic myelogenous leukaemia (CML) in the chronic phase; treatment of paediatric patients with chronic phase Philadelphia chromosome positive CML with resistance or intolerance to prior therapy including imatinib.

The Chair thanked those who had presented and attended the AWMSG Best Practice Day at Cardiff City Stadium on 10th July. Local initiatives had been shared with around 125 colleagues and it is hoped that these initiatives will be rolled out in other areas to improve prescribing and achieve better outcomes for patients. The Chair confirmed that presentations would be available via the AWTTC SHARE communication platform (which is available to all NHS staff via AWTTC), and the AWMSG website.

The Chair reminded members that this was his last AWMSG meeting. He confirmed there would be no meeting in August and the meeting in September would be chaired by Professor John Watkins whilst Welsh Government undertakes the public appoint process for a replacement. Dr Linton thanked members and AWTTC for their support over the years.

7. Appraisal 2: Full Submission

Dalbavancin (Xydalba®) for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults

The Chair welcomed delegates from Correvio UK Ltd.

The Chair invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chair announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on health boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published.

Dr Caron Jones, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the resubmission as outlined in the ASAR and comments received from clinical experts. It was noted that the marketing authorisation holder had proposed that the appraisal be restricted to a sub-population as opposed to the whole of the licensed indication. It was confirmed that the SMC had approved the medicine for the same restricted patient population for use in Scotland. Attention was drawn to the clinical expert comment that treatment would only be initiated on the advice of a microbiologist and never in empiric therapy.

The Chair invited the NMG Chair, Dr James Coulson, to relay relevant issues from the appraisal by NMG held on 13th June. Dr Coulson confirmed that based on evidence of clinical effectiveness and cost-effectiveness, and having taken the views of clinicians and patients into account, NMG had supported use of dalbavancin (Xydalba®) within NHS Wales for restricted use within the indication being appraised by AWMSG

The Chair opened discussion in relation to clinical effectiveness. There were no outstanding issues relating to the case for clinical effectiveness and the Chair moved to the case for cost-effectiveness. Professor Dyfrig Hughes clarified his role as AWMSG's health economist and provided an overview of the case for cost-effectiveness as outlined in the ASAR. He highlighted the limitations of the evidence and commented on the budget impact estimates.

The Chair opened discussion. Members discussed the cost differences and it was noted that the majority of the financial saving would be made by discharging patients from hospital earlier than comparator medicines. Members sought clarification in relation to any safety issues associated with discharging patients after three or four days. Members were reassured that most adverse events occur soon after the initial dose, are transient, not serious and do not normally require treatment. It was acknowledged that the medicine might be attractive to the outpatient parenteral antimicrobial therapy services. It was suggested that NHS Wales might need to monitor costs and the Chair reassured members that WAPSU would be monitoring usage. Members considered the criteria of the trial and noted the relapse rate.

Dr Chris Palmer confirmed that AWTTC had approached two patient organisations for comment but none had been received. Mr Palmer reiterated that reduced hospitalisation would be welcomed by patients and supported the development of a new antibiotic medicine. Mr Palmer sought reassurance that the recommendation wording proposed by NMG would be clear for prescribers.

The Chair referred to the response from Correvio UK 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 Chair 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 Chair closed the appraisal.

Appraisal decision subsequently announced in public:
The Chair confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Dalbavancin (Xydalba®) is recommended as an option for restricted use within NHS Wales.

Dalbavancin (Xydalba®) should be restricted for use in the following circumstances within its licensed indication for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults:

- **as a second-line treatment of ABSSSI; or**
- **when methicillin-resistant *Staphylococcus aureus* (MRSA) infection is suspected; or**
- **on the advice of local microbiologists or infectious disease specialists; and**
- **the patient is at first hospitalised due to ABSSSI and needs intravenous antibiotics but is allowed early discharge as they don't need further inpatient treatment.**

Dalbavancin (Xydalba®) is not recommended for use within NHS Wales outside of these circumstances.

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

8. Appraisal 3: Limited Submission

Ciprofloxacin (Cetraxal®) for the treatment of acute otitis externa in adults and children older than 1 year with an intact tympanic membrane, caused by ciprofloxacin susceptible microorganisms

The Chair welcomed delegates from Aspire Pharma Limited.

The Chair invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chair announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on health boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published. The Chair set the context of the limited submission and confirmed that only evidence of budgetary impact in comparison to the comparator product(s) should be demonstrated. It was confirmed 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 Stuart Keeping, the AWTTC Appraisal Lead, summarised the submission and relayed the key aspects as outlined in the ASAR. Dr Keeping highlighted that ciprofloxacin (Cetraxal®) is the first licensed product for the treatment of acute otitis externa in adults and children older than 1 year with an intact tympanic membrane, caused by ciprofloxacin susceptible microorganisms.

The Chair invited the NMG Chair, Dr James Coulson, to relay relevant issues from the appraisal by NMG held on 13th June. Dr Coulson confirmed that based on evidence of clinical effectiveness and consideration of the budget impact estimates, and having taken the views of clinicians into account, NMG had supported use of Ciprofloxacin (Cetraxal®) for the treatment of acute otitis externa in adults and children older than 1 year with an intact tympanic membrane, caused by ciprofloxacin susceptible microorganisms.

The Chair sought comments in relation to clinical effectiveness. The clinical expert stated that less frequent dosing might lead to increased compliance compared to other treatment options and this may lead to increased uptake compared to that estimated by the company. It was acknowledged that NICE guidelines recommends off label use. The company estimated that displacement of unlicensed medicines would provide cost savings to NHS Wales and improve governance. The

company estimated that uptake of the medicine would be small and use of the medicine would provide an overall cost saving due to displacement of more costly medicines. AWTTC confirmed that even if ciprofloxacin were to achieve a significantly larger market share than that initially estimated by the company, the budget impact in NHS Wales would be minimal thus members were reassured that if this medicine were to be supported for use by AWMSG there would be no major financial implications.

In concluding the discussion, the Chair 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 Chair closed the appraisal.

Appraisal decision subsequently announced in public:
The Chair confirmed that having read the evidence and considered the various issues that arose during the discussion, the following recommendation would be forwarded to Welsh Government:

Ciprofloxacin (Cetraxal®) is recommended as an option for use within NHS Wales for the treatment of acute otitis externa in adults and children older than 1 year with an intact tympanic membrane, caused by ciprofloxacin susceptible microorganisms.

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

Mr Roger Williams left the meeting.

9. Feedback from AWPAG Meeting held 21st March 2018

Ms Kath Haines summarised the issues discussed at the AWPAG meeting held in March and confirmed that a further meeting of this group had been held last week. She took members through the draft minutes (Enc 5) and the Chair commented on the busy workload. The Chair thanked AWPAG for driving the AWMSG work programme forward.

10. Primary Care Empirical UTI Treatment Guidelines

The Chairman welcomed Nick Reid, Consultant Antimicrobial Pharmacist and Robin Howe, Lead Consultant in Microbiology, from Public Health Wales. The updated empirical antimicrobial treatment guideline for urinary tract infections (UTIs) was presented to AWMSG for endorsement. Members were informed that the updates had taken into account increasing incidences of antimicrobial resistance in Wales and, by treating UTIs more effectively, it is hoped that the number of treatment failures, and hence progression to urosepsis, will decrease. The Chair opened discussion. Members welcomed the guideline. An issue in relation to the procurement of fosfomycin was raised and members were given assurances that the authors would seek clarification of this issue with Procurement. Professor Hughes confirmed that a number of comments had been relayed by him to the authors from Mrs Alison Hughes. It was confirmed that the comments had been relatively minor and the authors agreed to respond to Mrs Hughes. The Chairman closed discussion by confirming AWMSG's strong endorsement of the All Wales Antimicrobial Guidance Group's Primary Care Empirical UTI Guidelines 2018 subject to minor change to take into account the discussion around the table and issues raised by Mrs Hughes.

11. Review of the process for appraising orphan and ultra-orphan medicines and medicines developed specifically for rare diseases

Mrs Sabrina Rind, AWTTC Senior Pharmacist, presented a review of the process for appraising orphan and ultra-orphan medicines and medicines developed specifically for rare diseases (Enc 7). Members were informed that feedback from clinicians and patients had been positive. The policy enabled greater consideration of the clinical and patient context which might help AWMSG in considering societal issues. It was confirmed that as a result of the introduction of this policy the number of positive recommendations for medicines in these categories had increased. Members

were informed that consideration would be given to the introduction of ICER thresholds in line with NICE policy. Mrs Rind confirmed that this work would be undertaken by AWTTC in consultation with stakeholders. Members were informed that the introduction of cost-consequence analysis would be discussed initially via the TDA Partnership Group. Mrs Samuels confirmed that the policy would be updated in line with these recommendations by the end of 2018.

The Chair confirmed the date of the next meeting on Wednesday, 12th September 2018 in Cardiff and closed the meeting.