Enclosure No:	**1/AWMSG/1017**
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, 13th September 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 Catherine Bale	Hospital Consultant	
4.	Dr Anwen Cope	Healthcare professional eligible to prescribe	
5.	Mrs Ellen Lanham	Community Pharmacist	
6.	Prof Dyfrig Hughes	Health Economist	
7.	Mrs Louise Williams	Senior Nurse	
8.	Dr Sian Lewis	Welsh Health Specialised Services Committee	1-5
9.	Dr Emma Mason	Clinical Pharmacologist	
10.	Mrs Susan Murphy	Managed Sector Primary Care Pharmacist	
11.	Mr Rob Thomas	ABPI Cymru Wales	
12.	Mr Chris Palmer	Lay Member	
13.	Mr Roger Williams	Managed Sector Secondary Care Pharmacist	1-6
14.	Dr Jeremy Black	General Practitioner	
15.	Dr Mark Walker	Medical Director	

IN ATTENDANCE:
Dr Saad Al-Ismail, NMG Chair
Dr Robert Bracchi, CAPIG Chair
Mr Anthony Williams, Senior Pharmacist PAMS, AWTTC
Mrs Ruth Lang, Head of Liaison & Administration, AWTTC

AWTTC Leads:

Dr Caron Jones, Senior Scientist
Mrs Kath Haines, Head of WAPSU
Mr Richard Boldero, Senior Pharmacist
Mrs Claire Thomas, Senior Pharmacist

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

2. Apologies
Mr Stuart Davies, Finance Director

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.
Dr Sian Lewis joined the meeting.

5. **Chairman's Report**

The Chairman confirmed Welsh Government ratification of the following advice:

Adalimumab (Humira) is recommended as an option for use within NHS Wales for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adolescents from 12 years of age with an inadequate response to conventional systemic hidradenitis suppurativa (HS) therapy. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent to or lower than the WPAS price.

Cefuroxime (Aprokam) is recommended as an option for use within NHS Wales for the antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery.

Triamcinolone hexacetonide is recommended as an option for use within NHS Wales for the treatment of juvenile idiopathic arthritis.

Bevacizumab (Avastin) is not recommended for use within NHS Wales in combination with paclitaxel and cisplatin or, alternatively, paclitaxel and topotecan in patients who cannot receive platinum therapy, for the treatment of adult patients with persistent, recurrent, or metastatic carcinoma of the cervix.
The case for cost-effectiveness was not proven.

Emtricitabine/tenofovir disoproxil fumarate (Truvada) is not recommended for use within NHS Wales in combination with safer sex practices for pre-exposure prophylaxis to reduce the risk of sexually acquired HIV 1 infection in adults at high risk.
The case for cost-effectiveness was not proven.

Vismodegib (Erivedge) is not recommended for use within NHS Wales for the treatment of adult patients with symptomatic metastatic basal cell carcinoma, or locally advanced basal cell carcinoma inappropriate for surgery or radiotherapy.
The case for cost-effectiveness was not proven

The Chair confirmed that statements of non-endorsement due to non-engagement in the appraisal process had been published for:

Bezlotoxumab (Zinplava) for the prevention of recurrence of Clostridium difficile infection (CDI) in adults at high risk for recurrence of CDI

Chenodeoxycholic acid (Chenodeoxycholic acid Leadiant) for the treatment of inborn errors of primary bile acid synthesis due to sterol 27 hydroxylase deficiency (presenting as cerebrotendinous xanthomatosis) in infants, children and adolescents aged 1 month to 18

years and adults

Daratumumab (Darzalex) in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy

Eslicarbazepine acetate (Zebinix) Monotherapy for the treatment of partial-onset seizures, with or without secondary generalisation, in adults with newly diagnosed epilepsy

Parathyroid hormone (Natpar) as adjunctive treatment of adult patients with chronic hypoparathyroidism who cannot be adequately controlled with standard therapy alone

Ranibizumab (Lucentis) for the treatment of visual impairment due to choroidal neovascularisation not due to pathological myopia or wet age-related macular degeneration

Tenofovir alafenamide (Vemlidy) for the treatment of chronic hepatitis B in adults and adolescents (aged 12 years and older with body weight at least 35 kg)

Vandetanib (Caprelsa) for the treatment of aggressive and symptomatic medullary thyroid cancer in children and adolescents aged 5 years to 18 years with unresectable locally advanced or metastatic disease

The Chairman informed members that following the appraisal of desmopressin acetate (Noqdirna) for the treatment of nocturia due to idiopathic nocturnal polyuria in adults which was undertaken at the previous meeting in July, Ferring Pharmaceutical Ltd had submitted a request for a review of the decision. The Chairman informed the committee that after consideration of the reasons for the request it had been agreed that an opportunity should be afforded to Ferring Pharmaceuticals to re-present their case with a health economist present to respond to questions relating to the cost-effectiveness of the medicine. The Chairman reminded members that questioning should relate only to the licensed area under discussion and within the appropriate scope and parameters for AWMSG decision-making. The Chairman requested that members should not prejudge the case and should make a recommendation based on the evidence and having had further opportunity for full and open discussion. He opened appraisal proceedings.

6. Appraisal 1: Full Submission

Desmopressin lyophilisate (Noqdirna) for the treatment of symptomatic nocturia due to idiopathic nocturnal polyuria in adults

The Chairman welcomed delegates from Ferring Pharmaceuticals Ltd.

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

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

The Chairman 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 Caron Jones, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR. Dr Jones drew attention to the focus by the company on treating nocturia due to idiopathic nocturnal polyuria in people aged > 65, for whom treatment options are currently limited. Dr Jones confirmed there are no other licensed treatments currently available and there is an unmet need in this patient population. It was noted that the medicine has been recommended for restricted use in Scotland.

Dr Al-Ismail confirmed that NMG had appraised desmopressin lyophilisate (Noqdirna) on 7th June 2017 and recommended its use as an option within NHS Wales for the treatment of symptomatic nocturia due to idiopathic nocturnal polyuria in adults. It was noted that cost-effectiveness evidence was only provided for a subpopulation of patients aged over 65 and NMG recommended that AWMSG should restrict any recommendation to this sub-population.

Dr Jones relayed the view of clinical experts and referred to the summary of comments. She highlighted the unmet need and relayed the view of experts that there is no effective treatment for nocturia due to idiopathic nocturnal polyuria. Experts stated that desmopressin acetate (Noqdirna) could be given as first-line treatment together with advice on lifestyle modifications such as fluid restriction for at least four hours before going to bed.

The Chairman opened discussion in relation to clinical effectiveness and there was general discussion in relation to treatment versus lifestyle changes. Members noted the strong placebo effect and there were comments in relation to the different doses used in men and women. The company delegates were questioned on the statistical significance of the data and improvement rates. They provided clarification in relation to the terminology and differences between nocturia and nocturnal polyuria. There was discussion in relation to the potential impact on secondary care and the company delegates explained the set process for diagnosis, including use of bladder diaries. The delegates suggested that patients would already be in the health system and there would be minimal impact in primary care. There was general acknowledgement that pharmacological intervention would be unnecessary if lifestyle changes could make a positive impact. There were questions in relation to the two years stop review, safety profile of the medicine and test requirements. It was noted that off-licence treatments required on-going monitoring compared to three blood tests for patients on desmopressin acetate. It was confirmed that the tests and visits to the GP had been included in the costs. Dr Al-Ismail confirmed that the clinical expert who attended NMG had stated that only 5% of patients would need pharmacological intervention and the importance of the assessment process was reiterated.

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. Professor Hughes acknowledged that the model had been well constructed and he highlighted some limitations. He then moved on to the budget impact. It was noted that introducing this treatment would result in a cost saving to NHS Wales in year 1, but would increase over subsequent years to a total budget impact over five years of £914,425. There were no issues in relation to the budget impact. In the absence of Mr Stuart Davies, Finance Director representative, Dr Sian Lewis highlighted the opportunity cost. The Chairman reminded members that affordability is outside the remit of AWMSG.

The Chairman referred members to the two patient organisation questionnaires submitted by Bladder Health UK and Parkinson's UK in Wales. Mr Palmer relayed the views of patients. Members were told that nocturnal polyuria is under-reported so the true extent of the problem is likely to be underestimated. Patients describe their distress at the sleep disturbance, which results in fatigue, lethargy and irritability. Mr Palmer said that patients struggle to cope with the condition. The risk of falls and serious injury when getting out of bed was highlighted. Being

able to distinguish between an overactive bladder and nocturnal polyuria would be considered advantageous for patients as it would enable treatment to be targeted, which would result in an improved quality and fewer side effects from less appropriate unlicensed medication. Another advantage highlighted was the beneficial impact on relationships between the person and their carer. The potential financial savings for patients in care homes was noted. There we no other wider society issues of note. Mr Roger Williams joined the meeting and was informed that he would not be eligible to take part in the vote for this specific appraisal.

The Chairman referred to the response from Ferring Pharmaceuticals Ltd to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. The delegate read a closing statement thanking AWMSG for the opportunity to repeat the discussion. The company delegate highlighted the small patient population and unmet clinical need. The point was made that patients living in Wales would be disadvantaged if AWMSG did not support use of the medicine as it was widely available in the rest of the UK. 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:

Desmopressin acetate (Noqdirna) for the treatment of nocturia due to idiopathic nocturnal polyuria in adults is recommended for restricted use within NHS Wales.

Desmopressin acetate (Noqdirna) should be restricted for use in the following subpopulation within its licensed indication for the treatment of nocturia due to idiopathic nocturnal polyuria in adults aged over 65, for whom treatment options are currently limited.

Desmopressin acetate (Noqdirna) is not recommended for use within NHS Wales outside of this subpopulation.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded within five working days 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
Afamelanotide (Scenesse) for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP)

The Chairman welcomed delegates from Clinuvel 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 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 Caron Jones, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR. Dr Jones highlighted that afamelanotide is the first licensed medicine for the prevention of phototoxicity in adult patients with EPP. It was noted that there is a clear unmet need for treatment.

Dr Al-Ismail confirmed that NMG had appraised afamelanotide (Scenesse) on 3rd May 2017 for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP) and recommended that the medicine should not be available for use in NHS Wales as the case for cost-effectiveness had not been proven. Dr Al-Ismail stated that NMG acknowledged that this medicine satisfied the AWMSG criteria for ultra-orphan status.

The Chairman informed members that the applicant company, Clinuvel Pharmaceuticals Ltd, had requested a meeting of the Clinician and Patient Involvement Group (CAPIG) to identify and discuss in more detail any additional benefits of the medicine from both a clinician and patient perspective. It was reported that a CAPIG meeting had been held on Friday, 21st July and he invited the CAPIG Chairman, Dr Robert Bracchi, to provide an overview of the discussion. Dr Bracchi referred to the meeting summary that had been provided to members and published on the AWMSG website. He explained the severity of the condition and described the impact of this on patients and family life. He described the unmet need and confirmed that there are currently no effective or licensed treatments for this condition. He relayed the views of patients and described the intolerable pain, the impact on mental health and well-being, and the feeling of isolation and loneliness. He explained that patients are unable to undertake normal every day activities such as taking children to school, walking the dog, going on holidays or sporting activities. Dr Bracchi highlighted the benefit of afamelanotide and outlined the potential impact of the medicine on patients and their carers/family.

The Chairman thanked Dr Bracchi for his summary and reminded members of the rationale behind the inclusion of information from CAPIG. He opened discussion in relation to clinical effectiveness.

One member asked the company delegates why they did not use the validated DL-QI tool for measuring quality of life. The company explained that the standard tools for measuring quality of life did not seem appropriate for EPP; it was suggested by the company that these tools would not capture the patient experience. The company confirmed that the quality of life questionnaire developed for EPP (EPP-QoL) was still undergoing validation. The company was asked to comment on the placebo response seen in the clinical trials. Members explored alternative treatment options and the use of reflective sunscreen. Safety concerns were discussed in relation to liver problems. The company delegate stated that safety is taken very seriously and that safety is monitored closely. Concern was expressed that a lot of the data are driven by a small patient population (n = 15). The company delegate explained that the vast majority of patients in the trial would not expose themselves to sunlight; length of time exposure to sunlight was the primary endpoint. Members were informed that expert clinical and patient evidence had been taken into account and given weight by the licensing authority as an exceptional circumstance. The company delegate stated that the positive patient and clinical feedback is the driver behind the company's submission. Members asked about presentation of the genetic disorder and the paediatric treatment plan.

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. The company delegates were asked to explain their rational for selecting a DALY as the appropriate measure. The company stated they considered this to be the best model to capture the disease. Professor Hughes highlighted the limitations of the simplistic modelling and the company delegate stated they had presented a realistic case. The Chairman reminded members of the latitude in exploring the case for cost-effectiveness in view of the small patient population. The company estimated fifteen eligible patients in Wales. Dr Al-Ismail informed members that the clinical expert at NMG was of the view that there may be a number of patients who remain undiagnosed. The Chairman referred members to the budget impact estimates. Dr Sian Lewis drew members' attention to the high opportunity cost and referred to the uncertainties in the case presented.

The Chairman referred members to the patient organisation questionnaires submitted by British Porphyria Society and two individual patients. Mr Palmer relayed the views of patients and read out two patient testimonies. The testimonies echoed the patient views captured by the CAPIG summary, and highlighted the benefits that patients had experienced from receiving afamelanotide via the clinical trial programme. Members were informed that there is a large social media network amongst patients.

The Chairman referred to the response from Clinuvel Pharmaceuticals Ltd to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. The company delegate reiterated the unmet need and highlighted the innovative nature of the medicine for treating people with EPP. 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:

Afamelanotide (Scenesse) is not recommended for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP).

The case for cost-effectiveness has not been proven.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded within five working days 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. Feedback from AWPAG meeting held on 14th June 2017

Ms Kath Haines presented the minutes of the meeting and drew members' attention to work currently on-going. The Chairman thanked AWPAG for their input into the delivery of the AWMSG work programme.

9. 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 5 – principles and recommendations of the Medicines Identified as Low Priority for Funding in NHS Wales document for endorsement.

Mr Simms explained that the purpose of the paper was for AWMSG to review a list of medicines that offer a limited clinical benefit to patients and which were considered low priority for funding in NHS Wales. He provided the background and explained that the NHS Chairs and Chief Executives of NHS Wales had made a commitment to identify opportunities to

improve primary care prescribing and make recommendations to restrict the prescribing of 5-10 medicines considered as low priority for funding in NHS Wales. Mr Simms informed members that the work had been progressed via the Pharmacy Directors and was based on the priority areas identified by NHS Clinical Commissioners which were included in the NHS England Next Steps on the NHS Five Year Forward View. Mr Simms highlighted that the paper aims to reduce inappropriate variation in prescribing of medicines identified as low priority for funding across NHS Wales and will ensure that health boards and clinicians are able to make most efficient use of available resources. He sought the endorsement of AWMSG.

The Chairman opened discussion. Concern was expressed that advising on disinvestment of medicines may fall outside the remit of AWMSG. Concern was also expressed that the health economic evidence on which to advise NHS Wales in relation to these medicines had not been provided to AWMSG. Mr Simms highlighted the need for advice to be issued for NHS Wales to support prescribers. There were differing views – some members welcomed the document and others expressed an opinion that the document would have no impact. A suggestion was made to include advice on disinvestment in the medicines strategy 2018-2023 document currently in development. Mr Simms confirmed that the paper had been out for consultation but some members stated they had not had sight of it. Acknowledging that there was no consensus the Chairman confirmed that the paper would be deferred pending clarification of the issues.

10. National Prescribing Indicators 2016-17: Analysis of Prescribing Data to March 2017

Mrs Claire Thomas and Mr Richard Boldero presented an analysis of the National Prescribing Indicators (NPIs), for the final quarter of 2016-2017, to AWMSG for information. For the current year, 13 primary care NPIs focus on seven therapeutic areas and the reporting of adverse reactions to medicines via the Yellow Card Scheme, in addition to three NPIs for secondary care. Mrs Thomas highlighted that there had been improvements across Wales, in line with the aims of the indicators, for 10 of the 12 primary care NPIs with a threshold, compared with the equivalent quarter of the previous year. The two indicators which did not show an improvement were proton pump inhibitors, and gabapentin and pregabalin prescribing, which had both increased. It was noted that use of antibiotics continues to reduce, which is line with the aim of the antimicrobial NPIs. The percentage of GP practices in each health board meeting the annual target of one Yellow Card report per 2,000 GP practice population ranged from 10% to 50%. Yellow Card reporting for GP practices and health boards overall continues to increase.

For the secondary care NPIs the antibiotic surgical prophylaxis indicator value saw a decrease of 5% compared to the previous quarter, with 7% of patients receiving prophylactic antibiotics in elective colorectal surgery for greater than 24 hours. For the insulin prescribing and prescribing of biosimilars NPIs the quarter for comparison was the equivalent quarter of 2015-2016. In primary care and secondary care there were decreases of 0.67% and 7.22% respectively in the use of long-acting insulin analogues. For the prescribing of biosimilars NPI there was an increase in the use of the filgrastim biosimilars by 0.51% to 98.6%, and for infliximab biosimilar use there was an increase from 26.2% to 56.5%. The insulin glargine biosimilar saw an increase from 0.23% to 2.49%. All of these changes are in keeping with the aim of the NPIs.

Mrs Thomas informed AWMSG that the consultation for the 2018-2019 NPIs would take place in October and invited members to contribute.

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

Date of next meeting – Wednesday, 11th October 2017 in Cardiff.