Enclosure No:	**1/AWMSG/0617**
Agenda Item No:	**1** – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Draft minutes of the AWMSG meeting held Wednesday, 26th April 2017 commencing 10.30 am in the Park Inn Hotel, Cardiff North, Circle Way East, Llanedeyrn, Cardiff, CF23 9XF

VOTING MEMBERS PRESENT:

			Did not participate in
1.	Professor John Watkins	Chair & Consultant in Public Health Medicine	
2.	Dr Cath Bale	Hospital Consultant	
3.	Dr Anwen Cope	Healthcare professional eligible to prescribe	
4.	Mr Stuart Davies	Finance Director	
5.	Mr Stefan Fec	Community Pharmacist	
6.	Prof Dyfrig Hughes	Health Economist	
7.	Mrs Mandy James	Senior Nurse	
8.	Dr Pushpinder Mangat	Welsh Health Specialised Services Committee	
9.	Dr Emma Mason	Clinical Pharmacologist	
10.	Mrs Susan Murphy	Managed Sector Primary Care Pharmacist	
11.	Mr Bill Malcolm	ABPI Cymru Wales	
12.	Mr Chris Palmer	Lay Member	
13.	Mr John Terry	Managed Sector Secondary Care Pharmacist	
14.	Dr Jeremy Black	General Practitioner	
15.	Dr Mark Walker	Medical Director	

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

AWTTC Appraisal Leads:
Dr David Jarrom, Senior Scientist
Mrs Sabrina Rind, 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

The Chairman opened the meeting and welcomed members.

2. Apologies

Dr Stuart Linton

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. Chairman's Report

The Chairman confirmed that arrangements for AWMSG's 15 year anniversary conference to be held in Cardiff on 27th and 28th June were progressing. Invited speakers included Professor Sir Liam Donaldson, an international champion of patient safety and public health, and Mr Steve Williams, Senior Clinical Pharmacist at the Westbourne Medical Centre and The Adam Practice in Dorset. Each health board will be invited to share their best practice and experience of local initiatives that have led to improved prescribing in their area.

Members were informed that AWMSG has been given a regular column in the publication Welsh Pharmacy Review. Issue 32 features the first article on the background of AWMSG and how its conception has enhanced access to medicines.

The Chairman confirmed that the minutes of the AWPAG meeting held on 1st March 2017 had been included on the agenda for information.

The Chairman announced that the final appraisal recommendation announced at the previous meeting in relation to idelalisib (Zydelig) had been ratified by Welsh Government and published on the AWMSG website. Members were informed that ratification of advice relating to bevacizumab (Avastin) has not been received.

It was reported that Vertex Pharmaceuticals had lodged a request for independent review of AWMSG's recommendation in relation to ivacaftor (Kalydeco) on the grounds of 'process'. The Chairman confirmed that a Clinician and Patient Involvement Group (CAPIG) meeting has been scheduled for 16th May. He confirmed that following this meeting, AWMSG will be asked to review their final appraisal recommendation taking into account the additional information gathered by CAPIG.

The Chairman confirmed that in the absence of a submission, the following medicines cannot be endorsed for use within NHS Wales:

Eslicarbazepine acetate (Zebinix®) [AWTTC ref: 1214] as an adjunctive therapy in adolescents and children aged above 6 years, with partial-onset seizures with or without secondary generalisation.

Lacosamide (Vimpat®) [AWTTC ref: 1295] as monotherapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent (16–18 years) patients with epilepsy.

Ofatumumab (Arzerra®) [AWTTC ref: 2300] in combination with fludarabine and cyclophosphamide for the treatment of adult patients with relapsed chronic lymphocytic leukaemia

The Chairman confirmed that Welsh Government had issued a Welsh Health Circular (2017) 001 with new/revised Directions reflecting the new implementation timescales for medicines recommended for use by AWMSG and NICE.

Members were informed that the AWMSG meeting scheduled for 24th May in Cardiff has been cancelled. The next meeting will be held on Wednesday, 21st June. He announced the two appraisals scheduled:

Appraisal 1: Full Submission (Orphan/UO)
Afamelanotide (Scenesse) for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria
Applicant Company: Clinuvel Pharmaceuticals Ltd

Appraisal 2: Full Submission
Aviptadil phentolamine (Invicorp®) symptomatic treatment of erectile dysfunction in adult males due to neurogenic, vasulogenic, psychogenic, or mixed aetiology
Applicant Company: Evolan Pharma AB

Members were asked to contact AWTTC ahead of the next meeting with any personal or non-personal interests.

Patients, patient organisations and patient carers were invited to submit their views on medicines scheduled for appraisal via the AWMSG website or by contacting Ruth Lang at AWTTC.

6. Appraisal 1: Full Submission
Emtricitabine/tenofovir disoproxil fumarate (Truvada®) 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 Chairman welcomed delegates from Gilead Sciences 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 members 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. She provided an overview of the studies and highlighted that the medicine is the only licensed treatment for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in adults at high risk. Members were informed that the medicine can be accessed by patients in Scotland and is not currently available in NHSE. It was noted that some patients access the medicine via the internet and guidance on use is currently available. Mrs Rind drew members attention to a report published in March 2017 by the Welsh Independent HIV Expert Group which provided an overview of the current evidence related to the provision of PrEP for HIV prevention, featuring an extensive review of the available evidence, analysis of clinical trials, policy, regulatory and legislative content and global perspectives. Members were informed that the report had not been referenced in the ASAR as it had not been published at the time the ASAR was produced. Mrs Rind informed members that NHSE would be conducting a clinical trial which is expected to start in the Summer of 2017.

Dr Al-Ismail confirmed that an appraisal had been undertaken by NMG on 8th March 2017. He relayed NMG's recommendation to AWMSG that emtricitabine/tenofovir disoproxil fumarate should 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. It was the view of NMG that the case for cost-effectiveness had not been proven as there were several uncertainties and limitations in the economic model provided in the company's submission.

The Chairman asked Mrs Rind to relay the views of clinical experts. It was noted that five clinicians had submitted views, two of which had declared a personal specific interest. Mrs Rind confirmed that one clinical expert had been in attendance at the NMG meeting together with two representatives from Public Health Wales – the lead authors of the Welsh expert group report. Experts highlighted that no other treatment options are currently available to reduce the risk of sexually acquired infection in adults at high risk. It was noted that HIV prevention strategies include education and health promotion along with advice on condom use and sexual abstinence. Mrs Rind highlighted the strength of support from clinical experts for this treatment to be available in NHS Wales to address the unmet clinical need.

Mrs Rind reported clinical experts had confirmed that the PROUD study was most reflective of Welsh practice and they have confidence in the efficacy results of this study being transferable. Mrs Rind confirmed that clinical expert opinion had been sought on the baseline infection rate reported in the Welsh expert group report and in the PROUD study. It was suggested that the PROUD study was considered to be the most relevant to Welsh clinical practice; however, it was unclear why the baseline infection rates reported in the PROUD study were higher than the UK estimates. The clinical expert considered infection rates would be higher than those reported in the Welsh report but not as high as reported in the PROUD study. It was noted that the economic model is highly sensitive to the baseline infection rates and members noted that PrEP is only cost effective at the higher rates as described by the company in the PROUD study and not at the rates presented in the expert report for Wales. The company delegates stated that they did not accept that the baseline infection rates in the Welsh expert report for men who have sex with men who are tested for HIV and have been retested within one year accurately reflects the incidence in the high risk group. Mrs Rind reported that clinical experts advised that the clinical evidence detailing how long patients remain high risk is limited and unclear. The point was made by the company delegate that some patients have fluctuating periods of high risk behaviour and, if underlying problems are resolved, they may not continue to be high risk.

Members discussed the adherence rates and implications of non-adherence. Members explored whether or not treatment alone modified behaviour to affect the risk of infection. The company delegates suggested that a more comprehensive treatment package might encourage non-motivated patients to seek treatment. The point was made that taking drugs and alcohol alters a person's capacity to make good decisions. Attention was drawn to the evidence in the PROUD study indicating that treatment did not stop the high risk behaviour. Clarification was sought over the definition of 'high risk'. The Chairman asked the Wales Expert Group Public Health Wales lead author sitting in the audience whether there was potential for Wales to tie in with the trial to be undertaken in NHSE and it was confirmed that PHW is currently exploring involvement in the NHSE clinical trial.

The Chairman invited Professor Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed his role as the AWMSG health economist and confirmed that he had no involvement in the production of the ASAR and had not participated in discussions at NMG. Professor Hughes highlighted the limitations of the case for cost-effectiveness. He highlighted that the case presented by Gilead was that PrEP is a cost saving intervention in the majority of high-risk sub-populations with the exception of serodiscordant heterosexual couples. He pointed out that the length of time that a person may be considered high risk is

subject to change and the background infection rates used in the model are considerably higher than those suggested by other reports and Welsh Clinicians which impacts on the case for cost-effectiveness. Professor Hughes informed members that the uncertainties in adherence rates also have a detrimental impact on the case for cost-effectiveness as the economic evaluation assumes an adhering patient population.

The discussion moved on to the budget impact and the Chair asked members to consider the budget impact estimates in the ASAR. This was based on an estimate of 596 patients being treated per year with a cumulative medicine acquisition cost of £2,581,282 in year 1 and £12,923,734 in year 5. It was noted that cumulated risk had not been captured in the model as there was no robust way to capture this data. The company delegates confirmed that the figures are based on 12 months treatment duration

The Chairman sought clarification of the status of the clinical trial in NHSE and the company delegates responded to this request.

The Chairman confirmed that several patient organisation questionnaires had been received and, for the purposes of transparency, asked Mr Chris Palmer to relay the key issues highlighted in the submissions. Mr Palmer relayed the strong patient support. The organisations highlighted the primary advantage in that the medicine offers patients a reduced risk of acquiring HIV and a reduced risk of infecting others. The point was made that the cost of the medicine in preventing HIV would be less than the cost of treatment. The psychological complexities experienced by patients and adverse effects of the treatment of HIV were noted. Other advantages of the treatment, including ease of use, tolerability and good safety profile were relayed by Mr Palmer. Organisations referred to the World Health Organisation recommendation that PrEP should be made available immediately for those people at greatest need as it considered that PrEP is an effective and economic way to prevent the spread of HIV. There was discussion over the infection rates in Wales. The company delegates asked that the passionate feedback from patients be taken into consideration.

Having confirmed that there were no outstanding issues, the Chairman asked Gilead for their closing remarks. Confirmation was received that the appraisal process had been fair and transparent and that all relevant issues had been discussed. The Chairman closed the appraisal and members retired to vote in private.

The meeting re-convened and 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:

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 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.

7. Appraisal 2: Instructed Full Submission

Vismodegib (Erivedge®) for treatment of adult patients with symptomatic metastatic basal cell carcinoma, or locally advanced basal cell carcinoma inappropriate for surgery or radiotherapy

The Chairman welcomed delegates from Roche Products 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 confirmed that AWMSG's policy for appraising medicines for orphan, ultra-orphan medicines and medicines developed specifically for rare diseases had been tabled.

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 David Jarrom, AWTTC appraisal lead, set the context of the appraisal and highlighted the key aspects of the submission outlined in the ASAR. It was noted that the medicine had received its licence in 2013 and, as Roche Products had not engaged in the AWMSG appraisal process within the required timescale, a statement of non-endorsement had been published. Subsequently, in response to clinical demand the decision had been made by to pursue appraisal by AWMSG with or without engagement from Roche Products Ltd. Dr Jarrom confirmed that some clinical evidence and budget impact analyses had been provided by Roche; however, no evidence of cost-effectiveness had been forthcoming. It was noted that the medicine is not currently being marketed in the UK. Dr Jarrom explained that the situation in Scotland is similar to that in Wales in that the SMC had issued not recommended advice in the absence of a submission. He highlighted that the medicine is currently available in England via the CDF. Dr Jarrom confirmed that subsequent to the decision by the AWMSG Steering Committee to request appraisal by AWMSG, it had become apparent that NICE would be undertaking a technology appraisal. NICE advice on vismodegib is anticipated in November 2017.

Dr Al-Ismail confirmed that an appraisal by the NMG had been undertaken on 11th January 2017. He relayed the advice of NMG to AWMSG that vismodegib (Erivedge®) should not be 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. It was the view of NMG that the case for cost-effectiveness has not been proven as there was no cost-effectiveness evidence to support use of vismodegib (Erivedge®). Dr Al-Ismail confirmed that NMG considered that vismodegib (Erivedge®) satisfied the AWMSG criteria for ultra-orphan status.

Clarification was sought as to why a CAPIG meeting had not been convened. Dr Jarrom confirmed that AWTTC were unable to convene a meeting of CAPIG as there was no engagement from clinicians or patient organisations and a quorum could not be met. Mrs Samuels referred to the policy stating that a request for a CAPIG meeting is put forward by the 'applicant company' and Roche Products had not 'applied' for appraisal by AWMSG. Mrs Samuels informed members that for the benefit of potential patients AWTTC had attempted to convene a meeting.

The Chairman opened the discussion on clinical effectiveness. Roche delegates explained their rationale for not engaging in health technology appraisal and made the point that the medicine is not being marketed in the UK. The very rare indication and small number of eligible patients, coupled with a lack of evidence, formed the basis of their decision not to apply for HTA. It was

suggested that 8 patients in Wales would be eligible for treatment. The delegates explained that patients are not normally able to access oncology services and, because of this there is a lack of awareness of the treatment. The delegates explained that entry into the CDF predated the requirement to collect additional clinical outcome data and there is no on-going data collection. Members were informed that a final analysis of one long-term safety study would be available later this year, but no comparative studies were planned. The Roche delegates confirmed that a health economic model had been submitted to NICE.

The Chairman opened the discussion. Members explored the tolerability of vismodegib and the incidence rate of advanced basal cell carcinoma in Wales, which was acknowledged to be difficult to determine with any accuracy. The Chairman asked Dr Jarrom to relay the key points highlighted by clinical experts. It was noted that there is no standard therapy for these patient and treatment options are severely limited. Best supportive care which would include palliative treatment had been considered the most appropriate comparator. One expert highlighted an unmet need where a patient has inoperable disease or where radiotherapy cannot be administered. Another expert expressed a view that as most patients can be dealt with by surgery, in their opinion very few or no patients would require treatment with vismodegib.

Professor Hughes confirmed that as no case for cost-effectiveness had been provided he was unable to comment. He noted the availability of budget impact information. Total costs were estimated to be £970,000 in year 1, increasing to £1M in year 5: this was based on approximately 28 patients per year receiving treatment, and it was acknowledged that this may be an overestimate. The company delegates clarified that if sales data collected in England was extrapolated to the Welsh population, this would result in an alternative estimate of around 8 eligible patients in Wales.

Mr Chris Palmer informed members that three patient organisations had been invited to submit their views, but no responses had been received. The company delegates expressed disappointment that a CAPIG meeting had not been convened. There were no societal issues of note.

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:

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 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.

The Chairman closed proceedings.

8. Feedback from AWPAG Meeting held 1st March 2017
The draft minutes of the AWPAG meeting held 1st March 2017 were provided for information.

Date of next meeting – Wednesday, 21st June 2017 in Cardiff