Enclosure No:	**1/AWMSG/1216**
Agenda Item No:	**1** – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Draft minutes of the AWMSG meeting held Wednesday, 9th November 2016 commencing 9.30 am at the Park Inn, Cardiff North, CF23 9XF

VOTING MEMBERS PRESENT:			Did not participate in
1.	Dr Stuart Linton	Chair	
2.	Miss Anne Hinchliffe	Consultant in Pharmaceutical Public Health	
3.	Mr Stefan Fec	Community Pharmacist	
4.	Ms Pippa Anderson	Health Economist	
5.	Dr Sian Lewis	Welsh Health Specialised Services Committee	
6.	Dr Cath Bale	Hospital Consultant	
7.	Mrs Alison Hughes	Managed Sector Primary Care Pharmacist	
8.	Mr Chris Palmer	Lay Member	
9.	Mr John Terry	Managed Sector Secondary Care Pharmacist	
10.	Dr Jeremy Black	General Practitioner	
11.	Dr Mark Walker	Medical Director	
12.	Mr Stuart Davies	Director of Finance	
13.	Dr Emma Mason	Clinical Pharmacologist	
14.	Mrs Mandy James	Senior Nurse	

IN ATTENDANCE:
Dr Saad Al-Ismail, NMG Chair
Mrs Karen Samuels, Head of Patient Access to Medicines Service, AWTTC
Mrs Ruth Lang, Head of Liaison & Administration, AWTTC

AWTTC APPRAISAL LEADS:
Dr Caron Jones
Mrs Gail Woodland
Dr David Jarrom
Ms Kelly Wood
Miss Karen Jones

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
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, welcomed members and apologized for the slight delay in starting. The Chairman confirmed that the first two appraisals would be conducted in private as the submissions were associated with a Wales Patient Access Scheme and the meeting would subsequently be opened to the public.

2. Apologies

Professor Dyfrig Hughes (Ms Pippa Anderson deputising)
Professor John Watkins, Public Health Wales
Professor Stephen Monaghan, Public Health Wales

Dr Anwen Cope, healthcare professional eligible to prescribe
It was noted that there would be no representation from Welsh Government.

3. Declarations of interest

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

4. Minutes of previous meeting

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

5. Appraisal 1: Full Submission (WPAS)
Levofloxacin (Quinsair®) for the management of chronic pulmonary infections due to Pseudomonas aeruginosa in adult patients with cystic fibrosis

The Chairman welcomed delegates from Horizon Pharma plc. 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 confirmed that individuals in the public gallery were linked to AWTTC or the applicant company. The company delegates were reassured and the Chairman opened appraisal proceedings.

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 referred to the commercial sensitivities related to the medicine under appraisal and the comparator medicine, as both were associated with a Wales Patient Access Scheme. He reminded members that the price of the comparator medicine could not be divulged and, to protect commercial confidentiality, the applicant company delegates would be asked to leave the meeting for a few minutes to enable AWMSG to discuss the cost effectiveness and budget impact. The applicant company delegates and members agreed to this approach. The Chairman invited the AWTTC Appraisal Lead to set the context of the appraisal. Dr Caron Jones highlighted the key aspects of the submission outlined in the ASAR. She confirmed that the medicine is available in Scotland via health technology appraisal. Dr Sian Lewis confirmed that the comparator medicine is not commissioned in NHS England.

The Chairman invited Dr Al-Ismail to feed back the relevant issues identified in the preliminary appraisal. He confirmed that NMG had appraised levofloxacin (Quinsair®) on 5th October 2016 and supported it as an option for restricted use within NHS Wales. NMG considered that use should be restricted as a third-line therapy in patients who do not respond to, or are intolerant of, second-line treatment with tobramycin for the management of chronic pulmonary infections due to *Pseudomonas aeruginosa* in adult patients with cystic fibrosis. NMG did not support use outside of this subpopulation. Dr Al-Ismail relayed NMG's view that the medicine met the criteria for application of AWMSG's policy for appraising orphan, ultra-orphan medicines and medicines developed specifically for rare diseases.

The Chairman asked members to highlight any outstanding issues of clinical effectiveness. Clarification was sought in relation to the side effect profile. The company delegate confirmed that the company had committed to a long term safety study in the UK. The delegates were asked why the trial population had included children and adults, but the licence relates to the over 18 population only. The delegate confirmed that the number of children in the trial was considered insufficient and a new paediatric trial programme would be executed. A discrepancy in numbers in Table 1 was highlighted by a member and noted by Dr Jones. Members sought more information in relation to the long term and short term efficacy and safety data. It was noted there was no comparative head to head data in relation to the third-line comparator and

the company explained why this was the case. Members sought clarification as to whether altered taste had an impact on compliance and the company delegate confirmed that the impact had been minimal.

The Chairman referred to the summary of clinical expert views and Dr Jones emphasised the unmet clinical need for new therapeutics options to include in the monthly rotation of antibiotic treatment for patients with cystic fibrosis.

The Chairman invited Pippa Anderson to comment on the case for cost effectiveness. Ms Anderson confirmed that she is the NMG health economist and, on this occasion, she was deputising for Professor Dyfrig Hughes, the AWMSG health economist. She confirmed that she had no involvement in discussions at NMG or in the production of the ASAR. She summarised the key aspects of the case for cost effectiveness as outlined in the ASAR and congratulated the company on their evaluation given the small patient population. She confirmed that the sensitivity analyses had enabled AWMSG to explore the uncertainties and the scenarios had been convincing. It was noted that the methodology does not recognise the value of an additional antibiotic treatment option for patients. Ms Anderson acknowledged that the applicant company had provided a good case for cost effectiveness.

The company delegates left the room and members discussed the cost effectiveness and budget impact, and considered the level of discount offered by the applicant company compared to the alternative medicines. The delegates returned and the appraisal continued.

The Chairman confirmed that no patient questionnaires had been received and Mr Palmer listed the organisations that had been contacted. Mr Palmer reiterated the unmet clinical need and welcomed another treatment option for clinicians and patients. Other wider societal issues were noted in that treatment is cyclical and the medicine may be more convenient for patients in that it is given twice daily compared to the comparator medicine which is administered three times daily. The important issue of antimicrobial stewardship was acknowledged and cross border issues noted.

The Chairman asked the company delegates if they wished to comment or highlight any further points of discussion. The delegates thanked AWMSG for the questions and commented that the discussion had been good and interesting. 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:

Levofloxacin (Quinsair®) is recommended as an option for restricted use within NHS Wales. Levofloxacin (Quinsair®) should be restricted for use as a third-line therapy in patients who do not respond to, or are intolerant of, second-line treatment with tobramycin for the management of chronic pulmonary infections due to *Pseudomonas aeruginosa* in adult patients with cystic fibrosis. Levofloxacin (Quinsair®) 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 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 confirmed that the final appraisal recommendation would be announced later in public. Horizon Pharma plc delegates left the meeting. The Chairman announced that the meeting programme required change due to delays in public transport.

6. Chairman's report

The Chairman opened the meeting to the public. It was announced that Anne Hinchliffe would be stepping down from her role as AWMSG member and the Chairman recognised Anne's loyal and valuable contribution for many years on the New Medicines Group.

The Chairman announced that having received confirmation of Welsh Government ratification, the following advice had been disseminated to NHS Wales on 26th October 2016.

Insulin degludec (Tresiba®) is recommended as an option for restricted use within NHS Wales for the treatment of diabetes mellitus in adult patients where treatment with a basal insulin analogue is considered appropriate. Insulin degludec (Tresiba®) is not recommended for use within NHS Wales for the treatment of diabetes mellitus in adolescents and children from the age of 1 year.

Eltrombopag (Revolade®) is recommended as an option for use within NHS Wales for the treatment of chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients aged 1 year to <18 years who are refractory to other treatments (e.g. corticosteroids, immunoglobulins). 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.

In the absence of a submission from the holder of the marketing authorisation, lenalidomide (Revlimid®) cannot be endorsed for use within NHS Wales for the treatment of adult patients with relapsed or refractory mantle cell lymphoma.

The Chairman confirmed that an AWMSG Masterclass would be held on 23rd November for the pharmaceutical industry at the All Nations Centre in Cardiff.

The Chairman informed members that the Citizens Jury Report and the relevant extract from the minutes of the previous meeting had been submitted to Welsh Government and the AWMSG Steering Committee would be considering the recommendations.

The Chairman reported that AWMSG's Patient and Public Interest Group (PAPIG) had met on 18th October. PAPIG members had commented on the new AWTTC website and patient information leaflets currently in development. Updates on the implementation of recommendations following review of the Individual Patient Funding Request and the One Wales process had been provided. John Turner shared his experience on the Citizens Jury and AWTTC showed how PAPIG's views and suggestions had been incorporated into AWMSG's process for appraising orphan and ultra-orphan medicines, and medicines developed specifically for rare diseases.

The Chairman confirmed that a consultation response from AWMSG had been submitted to the Genomics Taskforce.

The Chairman announced the appraisals scheduled for the next AWMSG meeting in Cardiff on 7th December 2016:

Appraisal 1: Full Submission (WPAS)
Isavuconazole (Cresemba®) for the treatment of invasive aspergillosis and mucormycosis in patients for whom amphotericin B is inappropriate
Applicant Company: Basilea Pharmaceuticals Ltd

Appraisal 2: Full Submission (PAS)
Fingolimod (Gilenya®) a single disease modifying therapy in highly active relapsing remitting multiple sclerosis for adult patients with rapidly evolving severe relapsing remitting multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more Gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI
Applicant Company: Novartis Pharmaceuticals UK Ltd

Appraisal 3: Full Submission
Ferric maltol (Feraccru®) for the treatment of iron deficiency anaemia in adults with inflammatory bowel disease
Applicant Company: Shield Therapeutics

Appraisal 4: Limited Submission (WPAS)
Ivacaftor (Kalydeco®) for the treatment of cystic fibrosis in children aged 2 to less than 6 years weighing less than 25 kg who have one of the following gating (class III) mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R
Applicant Company: Vertex Pharmaceuticals UK Ltd

Appraisal 5: Limited Submission
Adalimumab (Humira®) for the treatment of moderately active Crohn's disease in paediatric patients (from 6 years of age) who have had an inadequate response to conventional therapy including primary nutrition therapy, and a corticosteroid and/or an immunomodulator, or who are intolerant to or have contraindications for such therapies
Applicant Company: AbbVie Ltd

Members were reminded to declare any interests in relation to these appraisals before the next meeting. Patients, patient organisations and patient carers were invited to submit their views on the medicines scheduled for appraisal.

7. Appraisal 2 (Appraisal 5 on the agenda): Full Submission
Dequalinium chloride (Fluomizin®) for the treatment of bacterial vaginosis

The Chairman welcomed delegates from Kora Healthcare. 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 invited the AWTTC Appraisal Lead to set the context of the appraisal. Miss Karen Jones highlighted the key aspects of the submission outlined in the ASAR and concluded her overview by highlighting that the medicine is available in Scotland for restricted use.

The Chairman invited Dr Al-Ismail to feed back the relevant issues identified in the preliminary appraisal. He confirmed that NMG had appraised dequalinium chloride (Fluomizin®) on 5th October 2016 and supported use as an option for restricted use within NHS Wales; dequalinium chloride (Fluomizin®) for the treatment of bacterial vaginosis is restricted for use after initial treatment is ineffective or not tolerated as an alternative option to clindamycin vaginal cream. It was noted that NMG were not supportive of use outside of this population.

The Chairman clarified the scope of the appraisal for second-line use and asked members to highlight any outstanding issues of clinical effectiveness. Clarification was sought regarding the absence of discharge in relation to clinical cure and the company delegates provided a comprehensive response. There was discussion in relation to comparator treatments and a comment was made by AWMSG's health economist that there had been a bold assumption of equivalence in terms of clinical benefits. She referred members to the issues highlighted in the ASAR and asked the company delegates to provide a rationale for this assumption. The Chairman referred to the summary of clinical expert views. Ms Jones relayed the key issues highlighted by experts, particularly the unmet clinical need as bacterial vaginosis is a very common condition with recurrence of symptoms being a particular issue which can also be psychologically distressing for patients.

The Chairman invited Ms Anderson to comment on the case for cost effectiveness. Ms Anderson confirmed her role as deputy for Professor Hughes, the AWMSG health economist and explained her role as NMG health economist. Ms Anderson confirmed that she had not been involved in the preliminary appraisal by NMG or in the production of the ASAR. She summarised the key aspects of the case for cost effectiveness as outlined in the ASAR and drew attention to the limitations of the evidence provided. The company delegate explained that Kora Healthcare had been explicit over the lack of evidence and it was confirmed that AWTTC had accepted the cost minimisation analysis at the scoping stage. The Chairman acknowledged that a pragmatic approach to the appraisal had been required. Members considered the budget impact and members recognised that some sensible assumptions had been made.

The Chairman confirmed that no patient questionnaires had been received and asked Mr Palmer to inform members of the organisations contacted for input during the appraisal process. Members considered wider societal issues and recognised the importance of patient choice in relation to treatment. The high level of resistance to treatment and use of over the counter medication was noted. The issue of antimicrobial stewardship was acknowledged in that the treatment offered an alternative to antibiotics. The psychological impact of the condition in relation to the unpleasant smell was recognised.

The Chairman asked the company delegates if they wished to comment or highlight any further points of discussion. The company delegates thanked members for the thorough discussion 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:

Dequalinium chloride (Fluomizin®) for the treatment of bacterial vaginosis is recommended as an option for restricted use within NHS Wales. Dequalinium chloride (Fluomizin®) for the treatment of bacterial vaginosis is restricted for use after initial treatment is ineffective or not tolerated as an alternative option to clindamycin vaginal cream. Dequalinium chloride (Fluomizin®) is not recommended for use within NHS Wales outside of this population.

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. Vitamins for Babies, Children and Pregnant and Breastfeeding Women

The Chairman invited Laura Low, Flying Start Dietitian and Helen Nicholls, Community Dietetics Services Manager, to present Enc. **4**/AWMSG/1116. Members were informed that the purpose of the guidance is to raise awareness amongst primary healthcare professionals and support staff of the recommendations for vitamin supplementation for babies, children, and pregnant and breastfeeding women, and their role in preventing vitamin deficiencies. The following outcomes were proposed:

- To increase the number of professional groups receiving the information.
- To increase the number of primary healthcare professionals and support staff aware of the recommendations on vitamins when surveyed annually.
- To increase uptake of Healthy Start vitamin vouchers (Welsh Government data).
- To increase uptake and continuation of vitamin supplementation (e.g. survey cohort of families).
- To increase the number of women receiving advice on appropriate vitamin supplements when surveyed annually.
- To increase the number of health boards with clearly defined policies on:
  - The effective distribution of Healthy Start vitamins.
  - Access to the recommended vitamin supplements for non-eligible families and women.

It was noted that the project relates to recommendation 4, 5 and 6 of AWMSG's Five Year Strategy 2013-2018. The wide consultation process was acknowledged.

The Chairman opened discussion and members welcomed the guidance. There was discussion over the short shelf life of the vitamins and it was confirmed that the authors would be working with Public Health Wales to overcome some of the issues relating to expiry dates. The authors also explained that they would be working with Pharmacy Education and Community Pharmacists to promote the guidance. The Chairman closed discussion by confirming AWMSG's unanimous support and endorsement of the guidance.

9 Review of existing advice:
Insulin detemir (Levemir®) for the treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above

Dr Jarrom explained that as part of the review process, AWTTC had considered a minor update to AWMSG's final appraisal recommendation to be required. Dr Jarrom confirmed that in the spirit of openness and transparency AWTTC had agreed that the FAR should be re-presented to AWMSG for approval prior to re-publication. Dr Jarrom confirmed that in line with AWMSG's review process there had been collaboration with the marketing authorisation holder and clinical experts. Members questioned the need for AWMSG approval prior to re-publication of reviewed advice, particularly in view of the minor change, and it was suggested that in future the updated FARs could be presented 'for information only'. Mrs Samuels agreed that AWTTC would reconsider the process in light of comments received. The Chairman confirmed AWMSG's approval of the updated FAR in relation to insulin detemir (Levemir®) for the treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above.

The meeting was closed to the public as the next agenda item would be an appraisal with an associated Wales Patient Access Scheme.

10. Appraisal 3 (Appraisal 2 on agenda) – Instructed by Welsh Government
Sofosbuvir/velpatasvir (Epclusa®) for the treatment of chronic hepatitis C virus (HCV) infection in adults

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 sought confirmation that individuals in the public gallery were there with the permission of the applicant company or AWTTC.

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 invited the AWTTC Appraisal Lead to set the context of the appraisal. Mrs Gail Woodland highlighted the key aspects of the submission outlined in the ASAR and highlighted that Welsh Government had requested appraisal of the medicine, which had met AWMSG's exclusion criteria in light of the impending appraisal by NICE. Members were informed that Gilead Sciences had provided evidence of clinical effectiveness and cost effectiveness in making a case to AWMSG to support use of sofosbuvir/velpatasvir in NHS Wales. It was noted that the medicine had been accepted for restricted use in Scotland.

The Chairman invited Dr Al-Ismail to feed back the relevant issues identified in the preliminary appraisal. He confirmed that NMG had appraised sofosbuvir/velpatasvir (Epclusa®) on 5th October 2016 and had supported its use as an option for the treatment of chronic hepatitis C virus infection in adults. It was the view of NMG that a positive recommendation should only apply 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 relayed NMG's view that use should be in accordance with the All Wales hepatitis C roll-out programme.

The Chairman asked members to highlight any outstanding issues of clinical effectiveness. Members sought clarification in relation to patient inclusion criteria in the ASTRAL-4 trial. Mrs Woodland relayed the view of the clinical experts and highlighted the key issues of the clinical expert summary. Experts stated that there is no non-interferon regimen for people with HCV genotype 3 infection who do not have significant fibrosis; they are currently treated with peginterferon plus ribavirin. A clinical view was expressed that interferon is difficult to take, has significant side effects and can cause significant health problems. Using interferon also limits the ability to treat patients, reduces the number of patients that can be treated and prevents treatment taking place in certain settings. It was noted that the UK has signed up to the World Health Organization hepatitis C eradication agenda.

The Chairman invited Ms Anderson to comment on the case for cost effectiveness. Ms Anderson confirmed her role as deputy AWMSG health economist. She confirmed that she had not been involved in the New Medicines Group's preliminary appraisal or the production of the ASAR. Ms Anderson summarised the key aspects of the case for cost effectiveness as outlined in the ASAR. She stated that the economic model attempts to accommodate the complexity of treatment. She highlighted the limitations of the evidence and explained that it created uncertainty but that the company had undertaken a range of sensitivity analyses to test the uncertainty. It was noted that the data in the model had been validated by experts. The company delegates acknowledged that selecting the most appropriate evidence to input into the model had been a challenge and a conservative approach had been taken. Members went on to consider the budget impact and the savings on drug acquisition costs were noted. It was noted that monitoring had not been included in the estimates and the company delegates confirmed that only serious adverse events had been factored into the calculations. There was recognition that the estimates appeared plausible. The company delegates confirmed the length of treatment is 12 weeks.

The Chairman confirmed that a patient questionnaire had been received from the Hepatitis C Trust, Hep C Positive - a voluntarily run support group and from an individual patient. Mr

Palmer summarised the key points that had been highlighted in the three responses. He relayed the view that the most significant advantage of Epclusa is its potential to widen access to interferon-free treatments to people who are not currently able to access such treatment. He stated that by curing hepatitis C, the medicine 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 highlighted that significantly shorter post treatment recovery times offer benefits to patients and enables individuals to resume normal family and working life. It was noted that improved tolerability has the potential to facilitate a significant increase in adherence rates. The medicine offers an opportunity to ease the emotional and psychological impact of the disease on the individual patient and their family/carers. The Chairman invited comment on other wider societal issues and the issue of access to medications via the internet was noted.

The Chairman asked the company delegates if they wished to comment or highlight any further points of discussion. They had no further comment 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:

Sofosbuvir/velpatasvir (Epclusa®) is recommended as an option for use within NHS Wales for the treatment of chronic hepatitis C virus 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 to 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.

The meeting was opened to the public.

11. National Prescribing Indicators 2016–2017 – Analysis of Prescribing Data to June 2016

Kath Haines, Head of WAPSU, presented Enc. **7**/AWMSG/1116 and highlighted the purpose of the document - to analyse data to June 2016 relating to AWMSG's National Prescribing Indicators (NPIs). Ms Haines explained that AWMSG's NPIs had been developed as a means of promoting safe and cost effective prescribing. Ms Haines confirmed that the 13 primary care NPIs focus on seven areas of prescribing and the reporting of adverse events (Yellow Cards). A threshold level of prescribing/reporting is set for 12 of the 13 primary care NPIs. Ms Haines drew attention to the 3 secondary care NPIs which had been newly introduced for 2016–2017. Ms Haines highlighted that 10 of the 12 pre-existing primary care NPIs demonstrated an improvement in prescribing, as measured by the Welsh average, compared to 2015–2016. It was noted that the report pertains to the 'Improving Health – Prescribing Guidance' recommendation in the AWMSG Five Year Strategy 2013–2018: *AWMSG will work with health boards and other stakeholders to promote the safe, effective and cost effective use of medicines in Wales.* The Chairman opened discussion. The increased use of biosimilars and financial savings were noted. Mrs Hughes referred to difficulties being experienced in reducing the level of pregabalin and gabapentin prescribing. The importance of sharing good prescribing practice was highlighted. Ms Haines informed members that the National Indicator Best Practice Day had been well received with excellent feedback from delegates. She confirmed AWTTC's intention to hold this event on an annual basis. The Chairman confirmed AWMSG's support of this. Ms Haines confirmed that the NPIs proposed for 2017/2018 were out

for consultation and would be presented to AWMSG at a future meeting.

12. Monitoring Usage in Wales of Medicines Appraised by NICE and AWMSG – Data to March 2016

Mr Richard Boldero, WAPSU Senior Pharmacist, presented Enc. **8**/AWMSG/1116. Mr Boldero explained the purpose of the document - to analyse the usage of medicines that have been appraised by the National Institute for Health and Care Excellence (NICE) and/or AWMSG. Members were informed that the report also includes medicines not appraised for use because a submission had not been received from the marketing authorisation holder, and therefore a Statement of Advice had been issued. Mr Boldero explained that the report monitors medicines appraised, and those for which a Statement of Advice has been issued, between April 2003 and 31 March 2016. It was noted that medicines usage data are reported for the period 1 April 2013 to 31 March 2016. The report was well received by members. Attention was drawn to the lack of use of some medicines which had been recommended by AWMSG as an option for use within NHS Wales. Members noted that £1.14M had been spent on medicines for which a Statement of Advice had been issued. Ms Haines confirmed that AWTTC is committed to developing an electronic application to monitor medicines usage and work is currently on-going comparing actual spend against projected spend. The Chairman closed discussion and thanked WAPSU for producing this useful resource.

13. Appraisal 4: Full submission
Aviptadil/phentolamine (Invicorp®) for the symptomatic treatment of erectile dysfunction in adult males due to neurogenic, vasculogenic, psychogenic, or mixed aetiology

The Chairman welcomed the delegates from Evolan Pharma AB. 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 invited the AWTTC Appraisal Lead to set the context of the appraisal and Dr David Jarrom highlighted the key aspects of the submission outlined in the ASAR. Dr Al-Ismail confirmed that NMG had appraised aviptadil/phentolamine (Invicorp®) on 5th October 2016 and did not support use within NHS Wales for the symptomatic treatment of erectile dysfunction in adult males due to neurogenic, vasulogenic, psychogenic, or mixed aetiology. Dr Al-Ismail confirmed NMG's view that the clinical and cost effectiveness data presented in the submission were insufficient for NMG to recommend its use.

The Chairman opened discussion and asked members to highlight any outstanding issues of clinical effectiveness. Members sought clarification over the use of the autoinjector. Professor Geoff Hackett, Consultant Urologist at Good Hope Hospital and Professor of Men's Health, Department of Diabetes at the University of Bedforshire explained that he had been involved in the trial and had been using aviptadil/phentolamine (Invicorp®) for many years. He stated that the autoinjector had been welcomed by patients involved in the trial. The holder of the marketing authorisation had considered the feasibility of marketing the autoinjector; however it had been considered too expensive. Professor Hackett explained that the main advantage of the medicine is that it is less painful to administer to patients who had undergone prostate surgery or radiotherapy. He described an intense burning pain and residual ache associated with the comparator and stated that pain is the major factor in determining patient preference. Professor Hackett highlighted the zero rate of priapism and convenience to patients in that they

can go home after the treatment is administered. Clarification was sought in relation to the selection of heterosexual adults in the trial. Dr Jarrom relayed the views of clinical experts who envisaged that aviptadil/phentolamine (Invicorp®) would be most suitable as an option where first-line treatment with PDE5 inhibitor(s) had failed. Clinical experts highlighted that for patients with severe erectile dysfunction, the simpler modalities of managing the condition are often unhelpful or sub-optimal. Other modalities of treatment are needed to treat all patients successfully.

The Chairman invited Ms Anderson to comment on the case for cost effectiveness. Ms Anderson confirmed her role in deputising for Professor Dyfrig Hughes. Ms Anderson confirmed that she had not been involved in the preliminary appraisal by NMG or in the production of the ASAR. Ms Anderson highlighted the limitations in the case presented for cost effectiveness. She explained that a CMA would only be accepted by AWMSG if equivalence could be demonstrated across all health domains and she expressed disappointment that the company had submitted a comparison of costs and it was not possible to have a meaningful discussion in relation to the medicine's cost-effectiveness. Ms Anderson suggested that omission of these important factors had led to the negative preliminary recommendation by NMG. The company delegates acknowledged the lack of investment in preparing a robust case for cost effectiveness and highlighted the high level of clinician and patient support for the medicine in England. The Chairman highlighted that AWMSG decisions are evidence based. The company delegate explained that the marketing authorisation holder is based outside the UK and he is the only UK employee. Mrs Samuels confirmed that AWTTC had offered support to the marketing authorisation holder and the appraisal lead had suggested ways to improve the submission.

Mr Palmer confirmed that one patient questionnaire had been received from the Sexual Advice Association. The patient group welcomed the medicine and stated that aviptadil/phentolamine (Invicorp®) would offer clinicians and patients an alternative treatment option when Caverject was considered to be too painful. The Chairman invited comment on wider societal issues. Professor Hackett reiterated the ease of administration, reduced side effect profile, cheaper price, patient and clinician support, low chance of priapism and no requirement for dose titration.

The Chairman asked the company delegate if he wished to comment or highlight any further points of discussion. The company delegate read out two testimonials from clinicians in England 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:

Aviptadil/phentolamine (Invicorp®) is not recommended for use within NHS Wales for the symptomatic treatment of erectile dysfunction in adult males due to neurogenic, vasculogenic, psychogenic, or mixed aetiology. The clinical and cost effectiveness data presented in the submission were insufficient for AWMSG to recommend its use.

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.

14. Appraisal 5: Limited Submission
Emtricitabine/rilpivirine/tenofovir alafenamide (Odefsey®) for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with human immunodeficiency virus 1 (HIV 1) without known mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) class, tenofovir or emtricitabine and with a viral load ≤ 100,000 HIV 1 RNA copies/mL

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 confirmed that the application had been considered eligible for a limited submission and no evidence of cost effectiveness is required. He stated that evidence of budgetary impact in comparison to the existing comparator product(s) should be demonstrated. The Chairman highlighted the importance of monitoring budget impact as AWMSG reserves the right to request a full submission if the budget impact exceeds that estimated in the submission.

The Chairman invited the AWTTC Appraisal Lead to set the context of the appraisal. Ms Kelly Wood highlighted the key aspects of the submission outlined in the ASAR. The Chairman invited Dr Al-Ismail to feed back the relevant issues identified in the preliminary appraisal. He confirmed that NMG had appraised emtricitabine/rilpivirine/tenofovir alafenamide (Odefsey®) on 5th October 2016 and supported use as an option for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with human immunodeficiency virus-1 (HIV-1) without known mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) class, tenofovir or emtricitabine and with a viral load ≤ 100,000 HIV-1 RNA copies/ml.

There were no outstanding issues of clinical effectiveness. Ms Wood highlighted that the medicine is currently recommended via HTA in Scotland. Ms Wood also relayed the views of clinicians and referred members to the summary of clinical expert views in the supporting documentation. Ms Wood stated an unmet clinical need had been identified in patients who would benefit from access to tenofovir alafenamide based single tablet regime which can be prescribed for patients with creatinine clearance > 30ml/min. The view of clinicians was that this medicine could be an extremely important new medicine for this group of patients and could enable them to achieve HIV virological suppression with a single tablet regimen.

The Chairman referred members to the estimated budget impact. There were no issues of note.

In the absence of a patient organisation questionnaire, Mr Palmer reiterated the need for new treatment options for patients. There were no wider societal issues of note.

The Chairman asked the company delegates if they wished to comment or highlight any further points of discussion. They had no further comment 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:

Emtricitabine/rilpivirine/tenofovir alafenamide (Odefsey®) is recommended as an option for use within NHS Wales for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with human immunodeficiency virus-1 (HIV-1) without known mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) class, tenofovir or emtricitabine and with a viral load ≤ 100,000 HIV-1 RNA copies/ml.

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.

15. Feedback from AWPAG Meeting held 28th September 2016

The Chairman invited Ms Kath Haines, Head of WAPSU, to present Enc. **11**/AWMSG/1116 – the draft minutes of the AWPAG meeting held on 28th September 2016. Ms Haines referred members to the meeting notes and highlighted that the NPIs paper, currently out for consultation, would be presented to AWMSG in February 2017. She confirmed that the CEPP had been updated and would also be presented to AWMSG in February 2017. Ms Haines confirmed that AWPAG had worked with the renal network in developing a CKD medicines management audit and this would be presented to AWMSG in December. Members were informed that the hypnotics and anxiolytics resource pack was under review and the patient information leaflet was in the process of being updated. The updated document would be presented to AWMSG in December along with the dry eye guideline document. There were no outstanding issues and the Chairman thanked AWPAG for developing the work programme.

The Chairman closed proceedings and confirmed the date of the next meeting:
Wednesday, 7th December 2016 in the Park Inn, Cardiff North.