Enclosure No:	**1/AWMSG/0916**
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 July 2016 commencing 9.30 am at Cardiff Metropolitan University, Llandaff Campus, Western Avenue, Cardiff CF5 2YB

VOTING MEMBERS PRESENT:

Did not participate in

1.	Dr Stuart Linton	Chair
2.	Prof John Watkins	Public Health Wales
3.	Mr Stephan Fec	Community Pharmacist
4.	Dr Karen Fitzgerald	Consultant in Pharmaceutical Public Health
5.	Prof Dyfrig Hughes	Health Economist
6.	Dr Sian Lewis	Welsh Health Specialised Services Committee
7.	Dr Sue Jeffs	Hospital Consultant
8.	Mrs Sue Murphy	Managed Sector Primary Care Pharmacist
9.	Mr Chris Palmer	Lay Member
10.	Mr Rob Thomas	ABPI Cymru Wales
11.	Dr Emma Mason	Clinical Pharmacologist
12.	Ms Anwen Cope	Healthcare Professional eligible to prescribe
13.	Mrs Louise Williams	Senior Nurse
14.	Mr Roger Williams	Managed Sector Secondary Care Pharmacist

WELSH GOVERNMENT:
No representation

IN ATTENDANCE:
Dr Saad Al-Ismail, NMG Chair
Mr Anthony Williams, Senior Appraisal Pharmacist – Team Leader, AWTTC
Mrs Ruth Lang, Head of Liaison & Administration, AWTTC

AWTTC APPRAISAL LEADS:
Dr Stephanie Francis, Senior Appraisal Scientist
Dr David Jarrom, Senior Appraisal Scientist
Ms Kelly Wood, Senior Appraisal Scientist
Mrs Sue Cervetto, Senior Appraisal 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
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 and welcomed members.

2. Apologies

Dr Mark Walker, Medical Director
Dr Cath Bale, Hospital Consultant
Mr Stuart Davies, Finance Director
Dr Jeremy Black, General Practitioner

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. Chairman's Report

The Chairman welcomed Anwen Cope who was attending her first meeting as an AWMSG member, having served on the New Medicines Group for a number of years as a representative from other healthcare professions eligible to prescribe. The Chairman informed members that Anwen is a dental practitioner with a research interest in the use of antibiotics for the treatment of dental problems in primary care. Members were informed that AWTTC had received the resignation of the deputy member, Mr Scott Cawley, and confirmed that AWTTC would be seeking a replacement at the earliest opportunity.

The Chairman expressed disappointment that it was Dr Karen Fitzgerald's last AWMSG meeting as her 8 year term of office had come to an end. He acknowledged Karen's support to AWMSG and its sub-groups since inception and expressed gratitude for her invaluable input over the years in representing Public Health Wales on the Group. The Chairman thanked Karen for her commitment and loyal service and confirmed that AWTTC is awaiting confirmation as to whether Miss Anne Hinchliffe, the deputy Public Health Wales representative, would step up from the New Medicines Group into the AWMSG member role.

The Chairman announced that the Citizens Jury project, held from 5th to 8th July in Cardiff City Hall had been delivered by Professor Marcus Longley and his team from the University of South Wales on behalf of AWMSG. The question posed to the jury was "How should patients and the public contribute to anti-microbial stewardship, and what support should the NHS offer them?" Members were informed that the jury had heard evidence over three days and formulated their verdict on the fourth day. The event had attracted interest from the media. The Chairman confirmed that a report would be written up by the University of South Wales and presented to AWMSG at a future meeting. The Chairman thanked all involved in the project.

The Chairman referred to his statement at the previous meeting that final NICE Highly Specialised Technology advice in relation to ataluren (Translarna®) for treating children aged 5 and over with Duchenne muscular dystrophy caused by a nonsense mutation was anticipated in July 2016. Members were informed that advice hadn't been published to date, and explained that on the basis that Welsh Health Specialised Services Committee had confirmed that there would be no barriers to its implementation, and in order to provide timely advice, AWMSG would be advising Welsh Government to implement the guidance in Wales once published.

The Chairman confirmed that of the six medicines being appraised, four had an associated patient access scheme. He confirmed that the meeting would close to the public following the second appraisal and announcement of the recommendations.

The Chairman highlighted that the draft minutes of the last meeting did not include AWMSG's recommendation relating to evolucumab (Repatha®) for the treatment in adults and adolescents with homozygous familiar hypercholesterolaaemia, in combination with other lipid-lowering therapies. The Chairman confirmed that the appraisal had been undertaken by AWMSG pending publication of final NICE guidance in relation to the heterozygous

hypercholesterolaemia and mixed dyslipidaemia indication. The Chairman confirmed that this had been published and AWMSG's positive recommendation had been forwarded to Welsh Government. The Chairman stated that ratification of this and the other appraisal recommendations announced at the June meeting remained outstanding and confirmed that once received AWTTC would inform the applicant companies and the service by email, and would upload the final appraisal recommendations to the AWMSG website.

The Chairman confirmed that no meeting would be held in August. He confirmed that Professor John Watkins would chair the next meeting to be held on Wednesday, 21st September 2016 in Abergavenny. The Chairman pointed out that the date of this meeting had changed from the original date of 14th September. Members were informed that the first appraisal would be undertaken in private as it has an associated Wales Patient Access Scheme; the meeting would subsequently open at 10.30 am and the remaining appraisals would be conducted in public.

Appraisal 1: Full Submission (WPAS)
Golimumab (Simponi®) for the treatment of adults with severe, active non radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C reactive protein and/or magnetic resonance imaging evidence, who have had an inadequate response to, or are intolerant to nonsteroidal anti-inflammatory drugs
Applicant Company: Merck Sharp & Dohme Ltd

Appraisal 2: Full Submission
Brivaracetam (Briviact®) as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent patients from 16 years of age with epilepsy
Applicant Company: UCB Pharma Ltd

Appraisal 3: Limited Submission
Rilpivirine (Edurant®) in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-naive patients from 12 years old to < 18 years old with a viral load ≤ 100,000 HIV-1 RNA copies/ml
Applicant Company: Janssen-Cilag Ltd

Appraisal 4: Limited Submission
Emtricitabine/tenofovir alafenamide (Descovy®) in combination with other antiretroviral agents for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with human immunodeficiency virus type 1 (HIV-1)
Applicant Company: Gilead Sciences Ltd

Appraisal 5: Full Submission
Green tea leaf extract (Catephen®) for the cutaneous treatment of external genital and perianal warts (condylomataacuminata) in immunocompetent patients from the age of 18 years
Applicant Company: Kora Corporation Ltd trading as Kora Healthcare

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 to AWTTC in relation to medicines scheduled for appraisal. The Chairman reminded members to sign and return the confidentiality statements to AWTTC.

6. Appraisal 1: Full Submission

Ceftolozane/tazobactam (Zerbaxa®) for the treatment of the following infections in adults: complicated intra-abdominal infections (cIAI); acute pyelonephritis; complicated urinary tract infections (cUTI). Consideration should be given to official guidance on the appropriate use of antibacterial agents

The Chairman welcomed representation from Merck Sharp & Dohme 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 outlined the sequence of events and invited the AWTTC Appraisal Lead to set the context of the appraisal.

Dr Jarrom highlighted the key aspects of the submission outlined in the ASAR. Dr Jarrom explained that the applicant company had focussed the application on a subgroup of patients within its licensed indication, that of patients with a confirmed cIAI or cUTI (including acute pyelonephritis) following non responsive first line therapy due to resistance, i.e. where susceptibility has been confirmed and ceftolozane/tazobactam is considered the most clinically appropriate option. He highlighted that the clinical evidence submitted by the company was not specific to this group of patients; all the studies included in the submission had inclusion criteria that allowed use of ceftolozane as a first-line/empiric therapy. Dr Jarrom confirmed that the view of clinical experts had been sought by AWTTC. Experts in Wales confirmed that the medicine would be prescribed by specialists in resistant patients and this broadly reflected the place in therapy proposed by the company.

The Chairman invited Dr Al-Ismail to feed back the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed that NMG had appraised ceftolozane/tazobactam (Zerbaxa®) on Wednesday, 8th June 2016 and had not recommended it for use for the treatment of complicated intra-abdominal infections; acute pyelonephritis and complicated urinary tract infections. Dr Al-Ismail stated that that the company had highlighted a sub-population of patients within the whole licensed indication where ceftolozane/tazobactam (Zerbaxa®) offered most benefit, but the case for clinical effectiveness had not been demonstrated in this sub-population of patients. He stated that NMG considered that the case for cost-effectiveness had not been proven.

The Chairman opened the discussion in relation to clinical effectiveness. Members sought clarification in relation to the novelty of the medicine and acknowledged the wider context of antimicrobial stewardship. It was noted that an independent body of UK clinicians recommended access to this medicine. The company delegates acknowledged the disconnect between the trial data and the potential positioning of the medicine in therapy. The Chairman acknowledged the difficulty that the use of conventional HTA presented to the company. Members explored the choice of comparator. An inaccuracy in the ASAR was highlighted in that the trial was described as ‘placebo controlled’ and Dr Jarrom agreed to correct this oversight. The ease of administration was noted. Clarification was sought in relation to the adverse effects.

The Chairman referred to the summary of clinical expert views and asked Dr Jarrom to highlight any key issues. Dr Jarrom explained the difficulty experienced in identifying the most appropriate comparators for the indications in this submission because of a divergence in guidelines across health boards in Wales. He confirmed the clinical expert view that the most appropriate comparators for the subgroup of patients highlighted in the submission are carbapenems (imipenem and meropenem) and piperacillin/tazobactam.

The Chairman invited Professor Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed his role as AWMSG health economist. Professor Hughes

summarised the case presented as outlined in the ASAR and highlighted the limitations in the submission. It was noted that cost-effectiveness was assessed only in the restricted subpopulation of patients outlined by the applicant company. The CMA assumed equivalence to the comparators; however Professor Hughes highlighted that ceftolozane/tazobactam is more costly in the base cases and in the majority of scenario/sensitivity analyses conducted. Members went on to consider and comment on the budget impact estimates and it was noted that the estimate incorporated cost differences resulting from the displacement of meropenem. There was discussion relating to the administration costs outlined in the ASAR. The company delegates confirmed that the estimates were based on discussion with clinicians, sales data and market research.

The Chairman confirmed that no patient organisation questionnaires had been received and, in the interests of transparency, asked the lay member, Mr Chris Palmer, to inform members of the organisations that had been approached by AWTTC. The Chairman reiterated that AWMSG's takes wider societal issues into account when making recommendations and invited any comments. There was discussion over the issue of antimicrobial stewardship, in particular the appropriate and responsible prescribing of antibiotics. The importance of developing new antibiotics to ensure the availability of a wide range of available treatments was also discussed. The implications of a positive and a negative recommendation were acknowledged.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegates to comment prior to concluding the appraisal. The company delegates provided a brief summary and thanked AWMSG for the broad discussion and involvement in the appraisal process.

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:

Ceftolozane/tazobactam (Zerbaxa®) is recommended as an option for restricted use within NHS Wales for the treatment of the following infections in adults: complicated intra-abdominal infections; acute pyelonephritis; and complicated urinary tract infections.

Ceftolozane/tazobactam (Zerbaxa®) is recommended only following non responsive first line therapy due to resistance, i.e. where susceptibility has been confirmed and ceftolozane/tazobactam is considered the most clinically appropriate option following Consultant Microbiologist advice.

Ceftolozane/tazobactam (Zerbaxa®) is not recommended for use within NHS Wales for use outside of this subgroup of patients.

Consideration should be given to official guidance on the appropriate use of antibacteral agents.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded within five working days. He informed company delegates that they had 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: Limited Submission

Aprepitant (EMEND®) for the prevention of nausea and vomiting associated with highly and

moderately emetogenic cancer chemotherapy in patients from the age of 6 months to less than 18 years old. Aprepitant is given as part of combination therapy

There was no representation from Merck Sharp & Dohme Ltd for this appraisal.

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 alluded to his previous statement 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 highlighted that the application had been considered eligible for a limited submission and there is no requirement on the applicant company to provide evidence of cost-effectiveness. Evidence of budgetary impact in comparison to the existing comparator product should be demonstrated and monitoring of the budget impact would be essential. The Chairman confirmed that AWMSG reserved the right to request a full submission if the budget impact exceeded that estimated in the submission.

The Chairman invited the AWTTC Appraisal Lead to set the context of the appraisal. Dr Jarrom highlighted the key aspects of the submission outlined in the ASAR. He explained that the application met the criteria for a limited submission as this is a minor licence extension for use in patients from the age of 6 months to less than 18 years old (aprepitant has been licensed in adults since 2003), and the anticipated usage of aprepitant is considered to be of minimal budgetary impact. The newly introduced oral suspension is also considered a significant new formulation. Dr Jarrom explained that aprepitant is administered in addition to, rather than instead of, a regimen that includes a 5-HT3 antagonist and a corticosteroid and the comparator is 'no additional treatment'.

The Chairman invited Dr Al-Ismail to feedback the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed that NMG had appraised aprepitant (EMEND®) on Wednesday, 8th June 2016 and recommended to AWMSG that it be used as an option within NHS Wales for the prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy in patients from the age of 6 months to less than 18 years old. Aprepitant should be given as part of combination therapy.

The Chairman asked members to highlight any outstanding issues of clinical effectiveness. None were raised. The historical absence of NICE or AWMSG advice for the licence in 2003 was noted. The Chairman referred members to the summary of clinical expert views and asked the appraisal lead to highlight salient issues. Dr Jarrom confirmed that clinicians welcomed the treatment. Dr Jarrom confirmed that children less than 12 years of age would be given the liquid formulation and children over the age of 12 would be given capsules. Tolerance issues in chemotherapy for children were acknowledged.

The Chairman confirmed that no patient organisation questionnaires had been received and asked the lay member, Mr Chris Palmer, to inform AWMSG members of the organisations that had been approached by AWTTC. Mr Palmer confirmed that seven patient organisations had been contacted by AWTTC and none had submitted views.

The Chairman referred members to the budget impact and there was discussion in relation to the number of aprepitant treatment cycles patients could be expected to receive. The Chairman referred to the applicant company's response and 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:

Aprepitant (EMEND®) is recommended as an option for use within NHS Wales for the prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy in patients from the age of 6 months to less than 18 years old. Aprepitant is given as part of combination therapy.

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 closed to members of the public to protect commercial confidentiality associated with subsequent appraisals.

8. Appraisal 3: Full Submission (WPAS)
Blinatumomab (Blincyto®) for the treatment of adults with Philadelphia chromosome negative relapsed or refractory B-precursor acute lymphoblastic leukaemia

The Chairman welcomed representation from Amgen Limited. The Chairman confirmed that all individuals remaining in the public gallery were part of AWTTC and asked the company delegates for permission to proceed with the appraisal.

The policy for appraising orphan and ultra-orphan medicines and medicines developed specifically for rare diseases was tabled along with the AWMSG policy for appraising medicines at the end of life.

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 alluded to his previous statement 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 outlined the sequence of events and 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. Ms Wood confirmed that the medicine had designated European Medicines Agency orphan status. In October 2015 the Committee for Orphan Medicinal Products reviewed the designation for blinatumomab (Blincyto®) as an orphan medicinal product for the treatment of acute lymphoblastic leukaemia and recommended that the orphan designation of the medicine be maintained. The applicant company considered that the AWMSG policy for appraising orphan, ultra-orphan medicines, and medicines developed specifically for rare disease should be applied to this appraisal. Ms Wood highlighted that approximately six patients would be potentially eligible for treatment in Wales. The applicant company were of the view that AWMSG's policy for appraising medicines at the end of life should be applied.

The Chairman invited Dr Al-Ismail to feedback the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed that NMG had appraised blinatumomab (Blincyto®) on Wednesday, 8th June 2016 and supported use within NHS Wales for the treatment of adults

with Philadelphia chromosome negative relapsed or refractory B-precursor acute lymphoblastic leukaemia. Dr Al-Ismail reiterated that this recommendation should apply only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price. It was noted that blinatumomab (Blincyto®) satisfied the AWMSG criteria for ultra-orphan drug status. NMG acknowledged that the AWMSG criteria for appraising life-extending, end-of-life medicines applied to blinatumomab (Blincyto®) for the indication under consideration.

The Chairman opened the discussion in relation to clinical effectiveness. Clarification was sought that the medicine was considered as a bridge to transplant rather than for palliative care. There was discussion over repeat cycles and adverse reactions. It was noted that no quality of life data had been collected in the study.

The Chairman referred to the summary of clinical expert views and asked Ms Wood to highlight any key issues. It was noted that an unmet need had been highlighted by clinical experts in Wales.

The Chairman invited Professor Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed his role as AWMSG health economist. Professor Hughes summarised the case presented as outlined in the ASAR and highlighted the key issues. The Chairman invited the company delegates to respond, but they had no comment. There was discussion in relation to the survival benefit at the tail end of the curve. The Chairman reiterated that the QALY is only part of a wider judgement of the value of the medicine and societal aspects would be an important component when appraising this medicine. Members considered the budget impact estimates and the potential cost to NHS Wales was noted.

The Chairman highlighted the important role of the lay member in ensuring that the patient, carer and public views and experiences inform the decisions of the Group. The Chairman asked all members to confirm they had received the patient organisation submission from Leukaemia CARE and asked Mr Palmer to briefly summarise the issues highlighted. Mr Palmer referred to the impact on patients both in their physical and psychological wellbeing. He highlighted the limited treatment options for patients and clinicians. It was noted that due to its mechanism of action this medicine has the potential to offer a number of quality of life benefits which could lead to improved outcomes, enhanced patient experience and enabling the patient to lead a more normal life following their diagnosis. Mr Palmer stated that improvements in a patient's treatment and quality of life will have a wider impact on the lives of their family and friends. The Chairman asked members to consider the wider societal issues and value that the medicine offered. It was acknowledged that this novel treatment may offer more time to patients, a more normal and better quality of life and a bridge to stem cell transplant.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegates to comment prior to concluding the appraisal. 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:

Blinatumomab (Blincyto®▼) is recommended as an option for use within NHS Wales for the treatment of adults with Philadelphia chromosome negative relapsed or refractory B-precursor acute lymphoblastic leukaemia.

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. He informed company delegates that they had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

9. Appraisal 4: Full Submission (WPAS)

Netupitant/palonosetron (Akynzeo®) in adults for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin based cancer chemotherapy and for the prevention of acute and delayed nausea and vomiting associated with moderately emetgenic cancer chemotherapy

The Chairman welcomed representation from Chugai Pharma UK Ltd and confirmed that individuals remaining in the public gallery were staff of AWTTC.

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 referred to his previous statement 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.

Dr Stephanie Francis highlighted the key aspects of the submission outlined in the ASAR. Dr Francis confirmed that the applicant company had focused their submission on the use of Akynzeo® for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based cancer chemotherapy and requested consideration of a restricted recommendation for this sub-population. Dr Francis confirmed that the comparator suggested by the applicant company is the combination of aprepitant (EMEND®) and ondansetron. Members were informed that clinical expert opinion concurred that this is the most widely used treatment for patients receiving highly emetogenic cisplatin-based chemotherapy. Dr Francis informed members that local guidelines from Velindre NHS Trust also state that aprepitant and ondansetron (plus dexamethosone) are the recommended first line anti-emetics for highly emetogenic cisplatin-based chemotherapy. Dr Francis confirmed that the applicant company submitted a cost-minimisation analysis (CMA) and, at the request of AWTTC, subsequently provided an additional cost-utility analysis (CUA) to strengthen their submission. It was noted that palonosetron solution for injection is not endorsed for use in NHS Wales and AWMSG had issued a statement of advice in June 2016 because the marketing authorisation holder had not engaged in the AWMSG appraisal process.

The Chairman invited Dr Al-Ismail to feedback the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed that NMG had appraised netupitant/palonosetron (Akynzeo®) on Wednesday, 8th June and supported the restricted use within NHS Wales for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based cancer chemotherapy. It was the view of NMG that netupitant/palonosetron (Akynzeo®) should not be recommended for use within NHS Wales for the prevention of acute and delayed nausea and vomiting associated with moderately emetogenic cancer chemotherapy. It was noted that the recommendation should apply only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price. Dr Al-Ismail informed members that the submission only included evidence of the cost-effectiveness of netupitant/palonosetron (Akynzeo®) for a subpopulation of

patients receiving highly emetogenic cisplatin-based chemotherapy.

The Chairman opened the discussion in relation to clinical effectiveness. Clarification of the terms 'highly' and 'moderately' was sought. It was noted that the licence states 'highly' emetogenic. The Chairman referred to the summary of clinical expert views and asked Dr Francis to highlight the key issues. Dr Francis confirmed that an unmet need had been identified and a clinical expert had highlighted that as palonosetron is not endorsed for use in NHS Wales there is currently no long-acting HT_3 inhibitor available for patients in Wales. The availability of netupitant/palonosetron would give patients access to a long-acting $5HT_3$ inhibitor and an NK_1 inhibitor in a convenient one-dose formulation.

The Chairman invited Professor Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed his role as AWMSG health economist. Professor Hughes summarised the case presented as outlined in the ASAR and highlighted the key issues. It was noted that Akynzeo® was dominant in both the CMA and CUA. Members were referred to the budget impact estimates and a potential cost-saving to NHS Wales was identified.

The Chairman confirmed that no patient organisation questionnaires had been received and asked the lay member, Mr Palmer, to inform AWMSG members of the organisations that had been approached by AWTTC. In the absence of any patient views, the Chairman reiterated that AWMSG's takes wider societal issues into account when making recommendations and invited comments. The convenience of use was noted.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegates to comment prior to concluding the appraisal. 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:

Netupitant/palonosetron (Akynzeo®) is recommended as an option for restricted use within NHS Wales for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based cancer chemotherapy.

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.

Netupitant/palonosetron (Akynzeo®) is not recommended for use within NHS Wales for the prevention of acute and delayed nausea and vomiting associated with moderately emetogenic cancer chemotherapy.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded within five working days. He informed company delegates that they had 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.

10. Appraisal 5: Full Submission (WPAS)
Lenalidomide (Revlimid®) for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant

The Chairman welcomed representation from Celgene Ltd. The Chairman confirmed that

individuals remaining in the public gallery were either part of AWTTC or Celgene Ltd and sought permission from the application company to proceed with the appraisal.

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 alluded to his previous statement 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 outlined the sequence of events and invited the AWTTC Appraisal Lead to set the context of the appraisal.

Mrs Cervetto relayed the key aspects of the submission outlined in the ASAR. Mrs Cervetto highlighted that the applicant company had requested that AWMSG considers lenalidomide in combination with dexamethasone for a specific subpopulation within the group of newly diagnosed patients with multiple myeloma who are not eligible for stem cell transplant; namely those patients within this subgroup who are unable to tolerate or have contraindications to thalidomide. Mrs Cervetto confirmed that the evidence submitted by Celgene was not limited to this sub-population. Mrs Cervetto relayed the view of AWTTC that lenalidomide may be eligible for consideration under the AWMSG policy for appraising orphan and ultra-orphan medicines and medicines developed specifically for rare diseases. The Chairman confirmed that this policy had been tabled for members' consideration.

The Chairman invited Dr Al-Ismail to feedback the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed that NMG had appraised lenalidomide (Revlimid®) on Wednesday, 8th June 2016 and recommended use as an option for restricted use within NHS Wales. It was the view of NMG that lenalidomide (Revlimid®) in combination with low-dose dexamethasone should be restricted for use within its licensed indication for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant in whom thalidomide is contraindicated or not tolerated. NMG were of the view that lenalidomide (Revlimid®) should not be recommended for use within NHS Wales outside of this subpopulation. Dr Al-Ismail highlighted that a positive recommendation should apply only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price. Dr Al-Ismail confirmed the view of NMG that the medicine satisfied AWMSG's criteria for a medicine developed specifically to treat a rare disease.

The Chairman opened the discussion in relation to clinical effectiveness. Clarification was sought in relation to the term 'unsuitable for thalidomide'. Members discussed the number of cycles and side effect profile. The Chairman referred to the summary of clinical expert views and asked Mrs Cervetto to highlight the key issues. It was the view of experts that lenalidomide would be used as an alternative to bortezomib in people with newly diagnosed multiple myeloma who were ineligible for transplant, particularly in people for whom an oral regimen would be more suitable, or those with pre-existing peripheral neuropathy or a contraindication to thalidomide. Mrs Cervetto confirmed the clinical expert view that lenalidomide may fulfil an unmet need as bortezomib is given subcutaneously, which requires weekly attendance at the haematology day unit for treatment. She stated that elderly patients and those with co-morbidities caused by myeloma itself can find weekly hospital visits difficult and suggested that an oral first line regime such as lenalidomide would meet this need. Mrs Cervetto clarified the clinical pathway as outlined by the clinical expert at the NMG meeting.

The Chairman invited Professor Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed his role as AWMSG health economist. Professor Hughes

summarised the case presented as outlined in the ASAR and highlighted the limitations of the cost minimisation analysis. Members considered the budget impact estimates.

The Chairman confirmed that a patient organisation questionnaire had been received from Myeloma UK and all members had received a copy. In the interests of transparency, the Chairman asked the lay member, Mr Palmer, to summarise the points highlighted from a patient, carer and public perspective. Mr Palmer highlighted that myeloma is an incurable, complex and destructive cancer of plasma cells. Whilst there is no cure, treatment can halt its progress for period of time and improve the quality of life for patients and their families. Mr Palmer highlighted the advantages of lenalidomide to patients in that; it improves survival for newly diagnosed patients; it has a lower incidence of peripheral neuropathy compared to treatments currently available; it is an oral treatment and reduces hospital visits and invasive infusions; it reduces the reliance on family members and carers; and improves psychological and emotional wellbeing. The advantages of an oral formulation were acknowledged, particularly for elderly patients. The Chairman reiterated that where the cost per QALY is above the normal thresholds, additional criteria for appraising the medicine may be applied and he referred members to these.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegates to comment prior to concluding the appraisal. The company delegates highlighted the benefits of the treatment, particularly in the older group of patients, and asked members to note the clinical setting. 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:

Lenalidomide (Revlimid®) is recommended as an option for restricted use within NHS Wales.

Lenalidomide (Revlimid®) in combination with low-dose dexamethasone should be restricted for use within its licensed indication for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant in whom thalidomide is contraindicated.

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.

Lenalidomide (Revlimid®) 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. He informed company delegates that they had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

11. Appraisal 6: Limited Submission (WPAS)
Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (Genvoya®) 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 any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir

The Chairman welcomed representation 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 confirmed 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 highlighted that the application had been considered eligible for a limited submission and there is no requirement on the applicant company to provide evidence of cost-effectiveness. Evidence of budgetary impact in comparison to the existing comparator product should be demonstrated and monitoring of the budget impact would be essential. The Chairman confirmed that AWMSG reserved the right to request a full submission if the budget impact exceeded that estimated in the submission.

The Chairman invited the AWTTC Appraisal Lead to set the context of the appraisal. Mrs Cervetto highlighted the key aspects of the submission outlined in the ASAR and confirmed that the appraisal focussed on a new formulation of an existing medicine at a pro-rata or reduced cost to the comparator. Mrs Cervetto relayed the views of the clinical experts and highlighted the improved side effect profile of Genvoya® in comparison to the existing medicine; due to the different prodrug to tenofovir contained within the single tablet combination (i.e. tenovofir alafenamide compared to tenofovir disoproxil fumarate). The importance of having access to a variety of medicines as it enables the clinicians to construct a treatment regime that is suitable for the vast majority of patients was expressed. Expert opinion suggested Genvoya® could fulfil an unmet need for those with renal dysfunction or at risk of toxic bone effects.

The Chairman invited Dr Al-Ismail to feedback the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed that NMG had appraised elvitegravir/cobicistat/emtricitabine/ tenofovir alafenamide (Genvoya®) on Wednesday, 8th June 2016 and recommended it for use as an option 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 any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir. Dr Al-Ismail highlighted that the recommendation should apply only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

The Chairman asked members to highlight any outstanding issues of clinical effectiveness. None were raised. The Chairman confirmed that no patient organisation questionnaires had been received and asked the lay member, Mr Chris Palmer, to inform AWMSG members of the organisations that had been approached by AWTTC.

The Chairman referred members to the budget impact and it was noted that the net budget impact based on the list price is zero for years one to five.

The Chairman referred to the applicant company's response and offered the opportunity to comment. Having received confirmation that the process had been fair and transparent he 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:

Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (Genvoya®) 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 any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir.

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. He informed company delegates that they had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

12. Date of next meeting

The Chairman confirmed the date of the next meeting on **Wednesday, 21st September 2016 in Abergavenny** and closed proceedings.