Enclosure No:	**1/AWMSG/1217**
Agenda Item No:	**4** – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Draft minutes of the AWMSG meeting held Wednesday, 8th November 2017 commencing 9.30 am in the Park Inn Hotel, Cardiff North, Circle Way East, Llanedeyrn, Cardiff, CF23 9XF

VOTING MEMBERS PRESENT:

			Did not participate in
1.	Dr Stuart Linton	Chair & Hospital Consultant	
2.	Professor John Watkins	Vice Chair & Consultant in Public Health Medicine	
3.	Dr Catherine Bale	Hospital Consultant	
4.	Dr Jeremy Black	General Practitioner	
5.	Mr Stuart Davies	Finance Director	
6.	Mr Stefan Fec	Community Pharmacist	
7.	Dr Sian Lewis	Welsh Health Specialised Services Committee	
8.	Prof Dyfrig Hughes	Health Economist	
9.	Mrs Alison Hughes	Managed Sector Primary Care Pharmacist	
10.	Mr Rob Thomas	ABPI Cymru Wales	
11.	Mr Chris Palmer	Lay Member	
12.	Mr Roger Williams	Managed Sector Secondary Care Pharmacist	

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

AWTTC Leads:
Dr Caron Jones, Senior Scientist
Dr Stuart Keeping, Senior Scientist
Mrs Claire Ganderton, Senior Pharmacist

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
ASAR	AWMSG Secretariat Assessment Report
AWMSG	All Wales Medicines Strategy Group
AWPAG	All Wales Prescribing Advisory Group
AWTTC	All Wales Therapeutics & Toxicology Centre
BMA	British Medical Association
CAPIG	Clinical and Patient Involvement Group
CEPP	Clinical Effectiveness Prescribing Programme
CHMP	Committee for Medicinal Products for Human Use
DoH	Department of Health
ECDF	English Cancer Drugs Fund
EMA	European Medicines Agency
EMIG	Ethical Medicines Industry Group
EOL	End of life
FAR	Final Appraisal Recommendation
FDA	US Food and Drug Administration
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health Boards
HST	Highly Specialised Technology
HTA	Health Technology Appraisal
IR	Independent Review
MHRA	Medicines and Healthcare products Regulatory Agency
MMPB	Medicines Management Programme Board
M&TCs	Medicines & Therapeutics Committees
NICE	National Institute for Health and Care Excellence
NMG	New Medicines Group
PAMS	Patient Access to Medicines Service
PAR	Preliminary Appraisal Recommendation
PAS	Patient Access Scheme
PPRS	Prescription Price Regulation Scheme
SMC	Scottish Medicines Consortium
SPC	Summary of Product Characteristics
TDAPG	Therapeutic Development Appraisal Partnership Group
T&FG	Task and Finish Group
UHB	University Health Board
WAPSU	Welsh Analytical Prescribing Support Unit
WCPPE	Welsh Centre for Pharmacy Postgraduate Education
WeMeReC	Welsh Medicines Resource Centre
WG	Welsh Government
WHO	World Health Organization
WHSSC	Welsh Health Specialised Services Committee
WPAS	Wales Patient Access Scheme

1. Welcome and introduction

The Chairman welcomed members. He confirmed that the first two appraisals would be conducted in private to maintain commercial confidentiality; thereafter, the meeting would be opened to the public.

2. Apologies

Dr Anwen Cope, Healthcare professional eligible to prescribe
Dr Emma Mason and Dr Balwinder Bajaj, Clinical Pharmacologist
Mrs Louise Williams and Mrs Mandy James, Senior Nurse
Dr Mark Walker, Medical Director

3. Declarations of interest

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

4. Minutes of previous meeting

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

5. The Chairman opened the appraisal session and reminded members that all appraisal questioning should fall within the appropriate scope and parameters for AWMSG decision-making, and should only relate to the licensed indication. The Chairman asked members to make recommendations based on the evidence provided and following full discussion. He referred members to the criteria for appraising orphan and ultra-orphan medicines and medicines developed specifically for rare diseases.

Appraisal 1: Full Submission (WPAS)

Pegvisomant (Somavert®) for the treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalize IGF-I concentrations or was not tolerated

The Chairman welcomed delegates from Pfizer Ltd and it was confirmed that individuals in the public gallery were staff of AWTTC and Welsh Government.

The Chair sought confirmation that members had access to the AWMSG policy for appraising orphan, ultra-orphan medicines and medicines developed specifically for rare diseases.

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

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

The Chairman explained that NMG had considered the clinical and cost-effectiveness issues in detail and had also taken account of clinical expert and patient views. He informed members there was no requirement to repeat this discussion. The Chairman asked members to highlight any outstanding clinical or cost-effectiveness issues and consider the company response to the preliminary recommendation. He explained that AWMSG would focus on the budget impact and wider societal issues.

Dr Caron Jones, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of this re-submission as outlined in the ASAR.

Dr Al-Ismail confirmed that NMG had undertaken an appraisal on 4th October and recommended pegvisomant (Somavert®) as an option for use within NHS Wales for the treatment of adult patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise insulin-like growth factor-1 (IGF-1) concentrations or was not tolerated. NMG advised 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 confirmed that NMG considered that pegvisomant (Somavert®) satisfied the AWMSG criteria for a medicine developed specifically for rare diseases as an ultra-orphan equivalent.

Dr Jones stated that clinical experts had highlighted an unmet need for the minority of patients who are not controlled by the current treatment options. Patients normally have disabling symptoms and comorbidities, leading to impaired quality of life and premature mortality. The view expressed by clinical experts was that it would be useful to have access to both pasireotide and pegvisomant in difficult-to-control cases. One expert highlighted inequity of access in the UK as pegvisomant had recently been made available to patients via commissioning in NHS England.

The Chairman opened discussion in relation to clinical effectiveness and members sought clarification in relation to the adverse reactions and availability of quality of life data. The company delegates explained the impact of normalising IGF-1 by reversing co-morbidities and soft tissue changes associated with the disease, with regression towards the norm. There was discussion in relation to life-expectancy, mortality outcomes and treatment resistance. Clarification was sought in relation to dosing and criteria for stropping treatment. The company delegates informed members of a European registry for data collection.

The Chairman invited Professor Dyfrig Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed that he took no part in the production of the ASAR and was in attendance as the voting health economist member of AWMSG. He summarised the evidence presented in the case for cost-effectiveness and highlighted the uncertainties in the modelling. The key issues outlined in the ASAR were highlighted. Professor Hughes commented on the budget impact estimates and highlighted potential cost savings. The Chairman acknowledged that the cost minimisation analysis presented AWMSG with a challenge and the company delegates explained the rationale for this approach. They considered that a cost-utility analysis would increase the uncertainty and complexity of the case for cost-effectiveness. Clarification was sought in relation to the choice of comparator and prevalence data.

The Chair reminded members that in line with AWMSG's policy for appraising orphan and ultra-orphan medicines members could apply a degree of latitude in relation to the cost per QALY. The company delegates were asked whether, given the small patient population, there was any scope to monitor the doses used in NHS Wales. They replied stating that they would check with the logistical department but could not make any commitment. It was noted that the average dose in Scotland is < 13 mg. Members recognised that with the high level of uncertainty, it would be important to review usage, cost and dose.

The Chairman referred members to the patient organisation questionnaire submitted by the Pituitary Foundation and asked the lay member, Mr Chris Palmer, to relay the key points. Mr Palmer stated that pegvisomant offered patients hope that their debilitating symptoms would improve and have a positive impact on their lives. The importance of patient choice was highlighted. Mr Palmer suggested that pegvisomant would offer an alternative treatment option to patients who would otherwise have to continue living with uncontrollable acromegaly. Mr Palmer referred to the patient quotes and highlighted the positive effects of the treatment. The importance of having a choice of treatment administration was acknowledged. Mr Palmer highlighted the small number of patients that would be eligible for treatment. The company delegates highlighted the homecare service provided which offers one nurse visit and subsequent telephone calls to provide advice and support regarding treatment administration.

The Chairman referred to the response from Pfizer Ltd to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. The delegates thanked AWMSG for the opportunity to input into the discussion and respond to questions. In concluding, the Chairman thanked the company delegates and, having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal. The company delegates left the meeting.

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:

Pegvisomant (Somavert®) is recommended as an option for use within NHS Wales for the treatment of adult patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise insulin-like growth factor-1 (IGF-1) concentrations or was not tolerated. 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.

6. Appraisal 2: Full Submission (WPAS)
Levodopa-carbidopa intestinal gel (Duodopa®) for the treatment of advanced levodopa-responsive Parkinson's disease with severe motor fluctuations and hyper-/dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results

The Chairman welcomed delegates from AbbVie Ltd. Confirmation was sought that only staff of AWTTC, AbbVie or Welsh Government remained in the public gallery.

The Chair sought confirmation that members had access to the AWMSG policy for appraising orphan, ultra-orphan medicines and medicines developed specifically for rare diseases. The policy criteria had been tabled.

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

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

The Chairman explained that NMG had considered the clinical and cost-effectiveness issues in detail and had also taken account of clinical expert and patient views. He informed members there was no requirement to repeat this discussion. The Chairman asked members to highlight any outstanding clinical or cost-effectiveness issues and consider the company response to the preliminary recommendation. He explained that AWMSG would focus on the budget impact and wider societal issues.

Dr Stuart Keeping, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR. He confirmed that the re-submission included additional evidence and a Wales Patient Access Scheme. Dr Keeping highlighted the inequity within the UK and confirmed that the medicine is currently available outside of Wales. He clarified the status as an ultra-orphan equivalent medicine.

Dr Al-Ismail confirmed that NMG had appraised levodopa-carbidopa intestinal gel (Duodopa®) on 4th October 2017 and recommended it as an option for restricted use for the treatment of advanced levodopa-responsive Parkinson's disease with severe motor fluctuations and hyper-

/dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results. NMG were of the view that levodopa-carbidopa intestinal gel (Duodopa®) should not be recommended for use within NHS Wales outside of this subpopulation. Dr Al-Ismail relayed the view 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. NMG considered that levodopa-carbidopa intestinal gel (Duodopa®) satisfied the AWMSG criteria for a medicine developed specifically for rare diseases as an ultra-orphan equivalent.

The Chairman clarified that the application focussed on a sub-population of the licensed indication.

The Chairman asked Dr Keeping to relay the views of clinical experts. Dr Keeping highlighted the unmet clinical need and informed members that there are no specific treatment guidelines in Wales. Clinicians stated that Duodopa® may be suitable for a very small number of patients with complex Parkinson's disease in the appropriate clinical circumstances when all other treatment options had been considered. Dr Keeping related the view of experts in Wales that treatment with Duodopa® can be difficult and it was noted that some clinicians may not have the requisite experience, knowledge or facilities available locally. The potential inequity between North and South Wales was noted. Dr Al-Ismail confirmed that from his experience in Oncology, insertion of the PEG tube (which is required for Duodopa®) would normally be performed by a gastroenterologist.

The Chairman opened the discussion in relation to clinical effectiveness. It was noted that the medicine would be less likely to be used by patients with dementia, those living in a care home or bed ridden. Dr Al-Ismail highlighted the multi-disciplinary approach to treatment. Clarification was sought in relation to the adverse drug reactions and safety profile. One member made the point that NICE had recommended that the medicine is not cost-effective and Mrs Samuels responded by confirming the non-mandatory status of NICE clinical guidelines within NHS Wales. The Chairman reiterated that NICE had not undertaken a health technology appraisal. Dr Keeping confirmed that NICE had looked at a wider patient population and the model submitted to AWTTC had been structured very differently to that submitted to NICE. The company delegates confirmed that patients do not develop resistance to the treatment.

The Chairman invited Professor Dyfrig Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed that he took no part in the production of the ASAR and was in attendance as the voting health economist member of AWMSG. He summarised the evidence presented in the case for cost-effectiveness. The Chairman reminded members of the latitude in relation to the ICER. The number of eligible patients and budget impact estimates were noted. It was noted that two patients currently receive the treatment via the individual patient funding request process and Mrs Samuels made the point that the budget impact would be less than the estimate in the ASAR as the patient access scheme would be applied.

The Chairman referred members to the two patient organisation questionnaires submitted by the Parkinson's UK in Wales and Cure Parkinson's Trust. Mr Palmer highlighted the complex nature of the disease which is characterised by a loss of an ability to move. Tremor makes fine movements virtually impossible; facial expression is lost, communication becomes problematic, swallowing can difficult, balance is severely impacted and there is a high propensity to fall. Hospital stays can be protracted, quality of life is slowly and painfully eroded. Mr Palmer stressed the importance of patient and clinician choice so that the appropriate treatment can be given at the appropriate time. The impact of adverse reactions in relation to all available treatment can be significant. Mr Palmer relayed the view of the patient organisation that the greatest unmet need in Parkinson's is a medication that slows, stops or reverses disease progression. The positive impact on the patient would have a significant effect on the carer, family and friends. It was noted that this treatment is not suitable for everyone; and the importance of treatment choice was reiterated. Mr Palmer informed members that Duodopa® reduces the burden and stress on

carers by decreasing the severity of symptoms which results in less supervision and eases the burden. The Chairman reiterated the unmet clinical need and rare disease consideration. Issues in relation to service provision with only two centres in Wales currently were noted.

The Chairman referred to the response from AbbVie Ltd to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. The company delegates thanked AWMSG for the opportunity to participate in the discussion. In concluding, the Chairman thanked the company delegates and, having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal. Members retired to vote in private and the meeting was opened to the public.

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:

Levodopa-carbidopa intestinal gel (Duodopa®) is not recommended for use within NHS Wales for the treatment of advanced levodopa-responsive Parkinson's disease with severe motor fluctuations and hyper-/dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results. The case for clinical and cost-effectiveness has not been proven.

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

7. Chairman's report

The Chairman confirmed Welsh Government ratification of the following AWMSG advice:

5-aminolaevulinic acid (Ameluz®) is recommended as an option for use within NHS Wales for the treatment of superficial and/or nodular basal cell carcinoma unsuitable for surgical treatment due to possible treatment-related morbidity and/or poor cosmetic outcome in adults.

C1 inhibitor (human) (Cinryze®) is recommended as an option for use within NHS Wales for the treatment and pre-procedure prevention of angioedema attacks in adults, adolescents and children (2 years old and above) with hereditary angioedema (HAE); routine prevention of angioedema attacks in adults, adolescents and children (6 years old and above) with severe and recurrent attacks of HAE, who are intolerant to or insufficiently protected by oral prevention treatments, or patients who are inadequately managed with repeated acute treatment.

Dolutegravir (Tivicay®) is recommended as an option for use within NHS Wales in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) infected adults, adolescents and children above 6 years of age.
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.

Glecaprevir/pibrentasvir (Maviret®) is recommended as an option for use within NHS Wales for the treatment of chronic hepatitis C virus (HCV) 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 or lower than the WPAS price.

Lenvatinib (Lenvima®) is recommended as an option for use within NHS Wales for the treatment

of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine (RAI). 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.

Tiotropium (Spiriva® Respimat®) is recommended as an option for use within NHS Wales as an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥ 800 micrograms budesonide daily or equivalent) and long-acting beta2-agonists and who experienced one or more severe exacerbations in the previous year.

In the absence of a submission from the holder of the marketing authorisation, dinutuximab beta (Dinutuximab beta Apeiron®) cannot be endorsed for use within NHS Wales for the treatment of high-risk neuroblastoma in patients aged 12 months and above, who have previously received induction chemotherapy and achieved at least a partial response, followed by myeloablative therapy and stem cell transplantation, as well as patients with history of relapsed or refractory neuroblastoma, with or without residual disease. Prior to the treatment of relapsed neuroblastoma, any actively progressing disease should be stabilised by other suitable measures. In patients with a history of relapsed/refractory disease and in patients who have not achieved a complete response after first line therapy, Dinutuximab beta Apeiron® should be combined with interleukin 2 (IL 2).

In the absence of a submission from the holder of the marketing authorisation, metformin hydrochloride (Glucophage SR®) cannot be endorsed for use within NHS Wales for the reduction in the risk or delay of the onset of type 2 diabetes mellitus in adult, overweight patients with IGT and/or IFG, and/or increased HbA1C who are: at high risk for developing overt type 2 diabetes mellitus and; still progressing towards type 2 diabetes mellitus despite implementation of intensive lifestyle change for 3 to 6 months. Treatment with Glucophage SR® must be based on a risk score incorporating appropriate measures of glycaemic control and including evidence of high cardiovascular risk. Lifestyle modifications should be continued when metformin is initiated, unless the patient is unable to do so because of medical reasons.

In the absence of a submission from the holder of the marketing authorisation, hydrocortisone sodium phosphate (Softacort®) cannot be endorsed for use within NHS Wales for the treatment of mild non-infectious allergic or inflammatory conjunctival diseases.

In the absence of a submission from the holder of the marketing authorisation, bevacizumab (Avastin®) cannot be endorsed for use within NHS Wales for use in combination with carboplatin and paclitaxel for the treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor–targeted agents.

In the absence of a submission from the holder of the marketing authorisation, sevelamer carbonate (Renvela®) cannot be endorsed for use within NHS Wales for the control of hyperphosphataemia in paediatric patients (> 6 years of age and a body surface area (BSA) of > 0.75 m2) with chronic kidney disease.

In the absence of a submission from the holder of the marketing authorisation, ledispavir/sofosbuvir (Harvoni®) cannot be endorsed for use within NHS Wales for the treatment of chronic hepatitis C in adolescents aged 12 to < 18 years.

In the absence of a submission from the holder of the marketing authorisation, maraviroc (Celsentri®) cannot be endorsed for use within NHS Wales in combination with other antiretroviral medicinal products for treatment-experienced adolescents and children of 2 years of age and older and weighing at least 10 kg infected with only CCR5-tropic HIV-1 detectable.

In the absence of a submission from the holder of the marketing authorisation, pentosan polysulfate sodium (Elmiron®) cannot be endorsed for use within NHS Wales for the treatment of bladder pain syndrome characterised by either glomerulations or Hunner's lesions in adults with moderate to severe pain, urgency and frequency of micturition.

The Chairman informed members that an independent review panel would be convened early in the New Year to investigate complaints submitted by Clinuval Pharmaceutial Limited following the announcement of AWMSG's recommendation on 13th September 2017 that afamelanotide (Scenesse) for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria is not supported for use within NHS Wales.

The Chairman reminded members of the consultations currently ongoing:

- National Prescribing Indicators 2018–2019
- All Wales Common Ailments Formulary
- All Wales Guide: Pharmacotherapy for Smoking Cessation
- AWMSG's Medicines Strategy 2018-2023

The Chairman reported an AWMSG Masterclass would be held in Cardiff on 22nd November 2017 and encouraged the pharmaceutical industry to attend and learn about the work of AWMSG and how to get the best outcome from AWMSG's health technology appraisal process.

The Chairman reported an AWMSG training day for member and deputies of AWMSG, NMG and AWPAG would be held on 17th January 2018 in Cardiff City Stadium.

The appraisal scheduled for the next AWMSG meeting to be held on 6th December 2017 in Cardiff was announced:

Adalimumab (Humira®) 40 mg solution for injection (pre-filled pen, pre-filled syringe and vial) for the treatment of paediatric chronic non-infectious anterior uveitis in patients from 2 years of age who have had an inadequate response to or are intolerant to conventional therapy, or in whom conventional therapy is inappropriate
Applicant Company: AbbVie Ltd

The Chairman asked members to contact AWTTC ahead of the next meeting if they had any personal or non-personal interests to declare. Patients, patient organisations and patient carers were invited to submit their views on the medicines to be appraised via the AWMSG website or by contacting Ruth Lang at AWTTC for further information on the appraisal process and future work programme.

8. Appraisal 3: Full Submission

Stiripentol (Diacomit®) in conjunction with clobazam and valproate as adjunctive therapy of refractory generalized tonic-clonic seizures in patients with severe myoclonic epilepsy in infancy (SMEI, Dravet's syndrome) whose seizures are not adequately controlled with clobazam and valproate

The Chairman welcomed delegates from Biocodex Ltd.

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

The Chairman announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on health

boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published.

The Chairman explained that NMG had considered the clinical and cost-effectiveness issues in detail and had also taken account of clinical expert and patient views. He informed members there was no requirement to repeat this discussion. The Chairman asked members to highlight any outstanding clinical or cost-effectiveness issues and consider the company response to the preliminary recommendation. He explained that AWMSG would focus on the budget impact and wider societal issues.

The Chairman sought clarification that all members had access to AWMSG's policy for appraising orphan, ultra-orphan medicines and medicines developed specifically for rare diseases.

Mrs Claire Ganderton, the AWTTC Appraisal Lead, set the context of the resubmission and relayed the key aspects of the ASAR. Mrs Ganderton highlighted that Dravet syndrome is a form of epilepsy that is typically resistant to treatment and that stiripentol is the only medicine licensed for the treatment of Dravet syndrome.

Dr Al-Ismail confirmed that NMG had appraised stiripentol (Diacomit®) on 4th October 2017 and recommended use in conjunction with clobazam and valproate as adjunctive therapy of refractory generalized tonic-clonic seizures in patients with severe myoclonic epilepsy in infancy (SMEI, Dravet syndrome) whose seizures are not adequately controlled with clobazam and valproate. Dr Al-Ismail relayed NMG's view that stiripentol (Diacomit®) satisfied the AWMSG criteria for a medicine developed specifically for rare diseases as an ultra-orphan equivalent.

The Chairman asked Mrs Ganderton to relay the views of clinical experts. Mrs Ganderton highlighted that clinical experts had confirmed that adjunctive stiripentol is already in use for treating Dravet syndrome in NHS Wales and has been for over 10 years. Experts also highlighted that, with the availability of genetic testing, patients are now being diagnosed at an earlier age, sometimes as young as 18 months. Mrs Ganderton confirmed that feedback from clinical experts supported the number of patients estimated to have Dravet syndrome in Wales, but that the proportion of those patients eligible for adjunctive stiripentol may be higher than that estimated by the company. Clinical expert feedback supports that the treatment pathway for treating patients with Dravet syndrome is not clearly defined, with stiripentol being added to a number of different dual therapy combinations, including valproate plus clobazam.

The Chairman confirmed that the case for clinical effectiveness had previously been met and no outstanding clinical issues were raised.

The Chairman invited Professor Dyfrig Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed that he took no part in the production of the ASAR and was in attendance as the voting health economist member of AWMSG. He summarised the evidence presented in the case for cost-effectiveness and commented on the budget impact estimates. Members sought clarification in relation to treatment over the age of 18 years. There was discussion in relation to the clinical presentation and rate of mortality in children. Clarification was sought in relation to the management and monitoring costs, the status epilepticus costs and in-patient costs.

The Chairman invited the lay member, Mr Chris Palmer, to relay the views of the patient organisation, Epilepsy Action Cymru. The organisation highlighted that Dravet syndrome is a very rare form of childhood epilepsy which affects a child's development, including speech and language. Mr Palmer stated that learning difficulties were very common in children with Dravet syndrome and can range from mild to very severe. The syndrome is one of the most resistant forms of epilepsy and several anti-epileptic medicines are not suitable. Mr Palmer highlighted that successful treatment with stiripentol (Diacomit®) could reduce the number of seizures, which

can often be severe, and fewer seizures would improve the quality of life of a child and have a positive impact on family life. The increased risk of premature death was noted.

The Chairman referred to the response from Biocodex to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. The company delegates highlighted the need to improve the quality of life for families. In concluding, the Chairman thanked the company delegates and, having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal. Members retired to vote in private.

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

Stiripentol (Diacomit®) is recommended for use within NHS Wales for use in conjunction with clobazam and valproate as adjunctive therapy of refractory generalized tonic-clonic seizures in patients with severe myoclonic epilepsy in infancy (SMEI, Dravet syndrome) whose seizures are not adequately controlled with clobazam and valproate.

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 the date of the next meeting on Wednesday, 6th December 2017 and closed the meeting.