Enclosure No:	**1/AWMSG/0516**
Agenda Item No:	**1** – Minutes of previous meeting
Author:	Chairman, AWMSG
Contact:	Tel: 029 20716900 E-Mail: awttc@wales.nhs.uk

ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Draft minutes of the AWMSG meeting held Wednesday, 20th April 2016 commencing 9.30 am at 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
2.	Professor John Watkins	Public Health Wales / Vice Chair
3.	Dr Jeremy Black	General Practitioner
4.	Mr Stefan Fec	Community Pharmacist
5.	Dr Karen Fitzgerald	Consultant in Pharmaceutical Public Health
6.	Professor Dyfrig Hughes	Health Economist
7.	Mrs Alison Hughes	Managed Sector Primary Care Pharmacist
8.	Mr Christopher Palmer	Lay Member
9.	Mr Rob Thomas	ABPI Cymru Wales
10.	Mrs Louise Williams	Senior Nurse
11.	John Terry	Managed Sector Secondary Care Pharmacist

WELSH GOVERNMENT:
Ms Karan Edwards

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

AWTTC APPRAISAL LEADS:
Dr Claire Davis, Senior Appraisal Scientist
Ms Kelly Wood, Senior Appraisal Scientist

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.

2. Apologies

Mr Scott Cawley (representing other professions eligible to prescribe)
Dr Mark Walker (Medical Director) & Dr Brendan Boylan (Medical Director)
Dr Sally Lewis (Welsh Health Specialised Services Committee)
Dr Cath Bale (Hospital Consultant)
Mr Stuart Davies (Finance Director)
Dr Emma Mason (Clinical Pharmacologist)

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. Mrs Samuels highlighted that Dr Fitzgerald's apologies had not been noted and agreed to update the draft minutes of the previous meeting.

5. Appraisal 1: Full Submission

Eribulin mesilate (Halaven®▼) for the treatment of patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments.

The Chairman welcomed representation from Eisai Ltd.

The Chairman confirmed the submission was associated with a Wales Patient Access Scheme (WPAS) and, to protect commercial confidentiality, the appraisal of this medicine would be conducted in private. The Chairman sought clarification that the individuals in the public gallery were related to AWTTC or Eisai Ltd and the applicant company delegates agreed that the appraisal should proceed.

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 Claire Davis highlighted the key aspects of the submission. Dr Davis explained that the company submission only provided clinical and cost-effectiveness evidence after two or more chemotherapies, within a post-capecitabine subpopulation. Dr Davis confirmed that NICE had previously assessed and not recommended the use of eribulin after two or more chemotherapies and that an updated submission had been provided to AWMSG. It was noted that the submission to AWMSG included a WPAS with further discount to NHS Wales and additional information. Dr Davis referred members to the AWMSG criteria for appraising life-extending, end-of-life medicines and AWMSG's policy for appraising orphan and ultra-orphan medicines and medicines developed specifically for rare diseases. Health economics, budget impact and wider societal issues were also highlighted.

The Chairman invited Dr Al-Ismail to feedback the relevant issues identified in the preliminary appraisal by NMG on 16th March 2016. Dr Al-Ismail confirmed that NMG recommended the restricted use of eribulin mesilate (Halaven®▼) as an option after at least two prior chemotherapeutic regimens for advanced disease which includes capecitabine. The view of NMG was that this recommendation should apply only in circumstances where the approved WPAS is utilised or where the list/contract price is equivalent or lower than the WPAS price. NMG did not recommend use of eribulin mesilate (Halaven®▼) outside of these circumstances. Dr Al-Ismail highlighted that the marketing authorisation holder only provided evidence of the clinical and cost-effectiveness of eribulin mesilate (Halaven®▼) within a subpopulation of patients (after at least two prior chemotherapeutic regimens, post-capecitabine) within the licensed indication. Dr Al-Ismail confirmed the NMG view that the AWMSG criteria for appraising life-extending,

end-of-life medicines did not apply to eribulin mesilate (Halaven®▼) for the indication under consideration. It was also highlighted that NMG considered that eribulin mesilate (Halaven®▼) satisfied the AWMSG criteria for appraising orphan and ultra-orphan medicines and medicines developed specifically for rare diseases.

The Chairman opened the discussion in relation to clinical effectiveness. Clarification was sought in relation to quality of life data and adverse events. Dr Davis highlighted clinical expert opinion, emphasising the unmet need for treatments that have a proven extension of overall survival and do not significantly impact on quality of life. Clinical experts had highlighted strong support for eribulin mesilate as an option for third- or fourth-line chemotherapy. It was noted that clinical experts were not concerned about neuropathy, as it is well-recognised and clinicians are used to managing it.

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 aspects.

The discussion led on to the budget impact. The assumptions in the budget impact were noted and members considered the number of patients that would be eligible for treatment within NHS Wales.

The Chairman reiterated that the cost per QALY is only part of a wider judgment of the value of this new medicine and reminded members that societal aspects would also be an important component in the appraisal. The Chairman highlighted the role of the lay member in ensuring that patient, carer and public views and experiences inform AWMSG. He referred members to the patient organisation questionnaire from the Breast Cancer Now and confirmed that all members had received and read the documentation. For the purposes of transparency the Chairman asked Mr Palmer to highlight the salient aspects of the patient questionnaire.

The Chairman drew members' attention to considerations relating to the AWMSG policy on appraising life-extending, end-of-life medicines and the process for appraising orphan and ultra-orphan medicines, and medicines developed specifically for rare diseases, asking members if there were any outstanding wider societal issues of note.

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:

Eribulin mesilate (Halaven®▼) is licensed for the treatment of adult patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments.

Eribulin mesilate (Halaven®▼) is recommended as an option for restricted use within NHS Wales after at least two prior chemotherapeutic regimens for advanced disease which includes capecitabine.

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.

Eribulin mesilate (Halaven®▼) is not recommended for use within NHS Wales outside of these circumstances.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies 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.

6. Chairman's report

The Chairman reported that subsequent to his announcement at the previous meeting, the appraisal of guanfacine (Intuniv®) for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents had been postponed. The applicant company, Shire Pharmaceuticals Ltd, had submitted information which had not been considered by NMG. AWTTC advised that NMG should have the opportunity to review this information prior to the appraisal by AWMSG which has been rescheduled to May.

The Chairman confirmed receipt of ministerial ratification in relation to the following recommendations:

Ivermectin (Soolantra®) is recommended as an option for use within NHS Wales for the topical treatment of inflammatory lesions of rosacea (papulopustular) in adult patients.

Oseltamivir (Tamiflu®) is recommended for use within NHS Wales for the treatment of infants less than 1 year of age including full term neonates who present with symptoms typical of influenza, when influenza virus is circulating in the community. Efficacy has been demonstrated when treatment is initiated within two days of first onset of symptoms.

Ustekinumab (Stelara®) is recommended as an option for use within NHS Wales for the treatment of chronic moderate to severe plaque psoriasis in adolescent patients from the age of 12 years and older, who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.

Tiotropium (Spiriva® Respimat®) is not recommended 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 $beta_2$ agonists and who experienced one or more severe exacerbations in the previous year. The company submission did not present sufficient evidence to demonstrate that tiotropium (Spiriva® Respimat®) is cost-effective.

Ulipristal acetate (Esmya®) is recommended as an option for use within NHS Wales for the intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age.

Prucalopride (Resolor®) is recommended as an option for use within NHS Wales for the treatment of chronic constipation in men in whom laxatives fail to provide adequate relief.

Sorafenib (Nexavar®) is recommended for restricted use within NHS Wales in the following circumstances for the treatment of hepatocellular carcinoma: patients with advanced hepatocellular carcinoma for whom surgical or loco-regional therapies have failed or were not suitable. 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. Sorafenib (Nexavar®) is not recommended for use within NHS Wales outside of these circumstances.

In the absence of a submission from the holder of the marketing authorisation, the following medicines cannot be endorsed and therefore should not be prescribed routinely within NHS Wales:

Aflibercept (Eylea®) for the treatment of patients with visual impairment due to myopic choroidal neovascularisation

Daptomycin (Cubicin®) for the treatment of paediatric (1 to 17 years of age) patients with complicated skin and soft-tissue infections

Glycerol phenylbutyrate (Ravicti®) adjunctive therapy for chronic management of adult and paediatric patients ≥ 2 months of age with urea cycle disorders including deficiencies of carbamoyl phosphate-synthase-I (CPS), ornithine carbamoyltransferase (OTC), argininosuccinate synthetase (ASS), argininosuccinate lyase (ASL), arginase I (ARG) and ornithine translocase deficiency hyperornithinaemia-hyperammonaemia homocitrullinuria syndrome (HHH) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone

Isavuconazole (Cresemba®) for the treatment of invasive aspergillosis and mucormycosis in patients for whom amphotericin B is inappropriate

Methoxyflurane (Penthrox®) for the emergency relief of moderate to severe pain in conscious adult patients with trauma and associated pain

Secukinumab (Cosentyx®) alone or in combination with methotrexate for the treatment of active psoriatic arthritis in adults when response to previous disease modifying anti rheumatic drug (DMARD) therapy has been inadequate

The Chairman announced the appraisals scheduled for the next AWMSG meeting to be held on Wednesday, 18th May 2016 in Cardiff:

Appraisal 1: Full Submission
Pasireotide (Signifor®) for the treatment of adult patients with acromegaly for whom surgery is not an option or has not been curative and who are inadequately controlled on treatment with another somatostatin analogue
Applicant Company: Novartis Pharmaceuticals UK Ltd

Appraisal 2: Full Submission
Guanfacine (Intuniv®) for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents 6 to 17 years old for whom stimulants are not suitable, not tolerated or have been shown to be ineffective. Intuniv must be used as a part of a comprehensive ADHD treatment programme, typically including psychological, educational and social measures
Applicant Company: Shire Pharmaceuticals Ltd

Appraisal 3: Full Submission
Dulaglutide (Trulicity®) indicated in adults with type 2 diabetes mellitus to improve glycaemic control as: monotherapy when diet and exercise alone do not provide adequate glycaemic control in patients for whom the use of metformin is considered inappropriate due to intolerance or contraindications; as add on therapy in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control
Applicant Company: Eli Lilly & Co 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 to AWTTC in relation to medicines scheduled for appraisal.

7. Appraisal 2: Limited Submission
Ursodeoxycholic acid (Ursofalk®) 250 mg hard capsules, 250 mg/5 ml suspension, 500 mg film-coated tablets for the treatment of hepatobiliary disorders associated with cystic fibrosis in children aged 1 month to 18 years

The Chairman acknowledged that there was no representation from Dr Falk Pharma UK 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 informed members that the application had been considered eligible for a limited submission and no cost-effectiveness information is required. He confirmed that the marketing authorisation holder would be expected to provide evidence of budgetary impact in comparison to the existing comparator product/s. The Chairman reiterated that monitoring of budget impact would be essential and AWMSG reserved to right to request a full submission if the budget impact exceeded that estimated in the submission.

The AWTTC appraisal lead, Kelly Wood, presented a brief summary of the ASAR and highlighted the key aspects of the submission. Members were informed that the limited submission criteria were met based on an estimated small difference in cost compared to comparators and an anticipated minimal budgetary impact in NHS Wales. The Chairman asked Dr Al-Ismail to feedback from the NMG preliminary appraisal held in March. It was confirmed that at the NMG meeting held on 16th March 2016, the Group had supported use of ursodeoxycholic acid (Ursofalk®) for use within NHS Wales for the treatment of hepatobiliary disorders associated with cystic fibrosis in children aged 1 month to 18 years.

Members were invited to seek clarification of any outstanding issue. One member highlighted the Cochrane review (2010) which was subsequently reviewed in (2014) which concludes there was insufficient evidence to justify routine use of ursodeoxycholic acid (UDCA) in cystic fibrosis. Kelly Wood made reference to the evidence that the licensing authority considered which included a study looking at the role of UDCA on the histological changes in children with cystic fibrosis liver disease. The licensing authority found the methodology of this study to be of great value as it looked at liver biopsy as well as ultrasound to assess the degree of liver disease. Reference was also made to local and international guidelines which recommend the use of UDCA to delay the progression of cystic fibrosis liver disease.

Dr Al-Ismail highlighted that experts have been using this product off-label for years in children and adolescents.

The Chairman reiterated the role of the lay member in ensuring that patient, carer and public views and experiences inform AWMSG. Mr Palmer confirmed that a patient organisation submission had been received from the Child Liver Disease Foundation and he highlighted the key issues.

Members then moved on to discuss issues relating to the budget impact. Kelly Wood gave an overview on the budget impact scenario presented by the company which demonstrated a net cost saving to NHS Wales.

There were no wider societal issues of note.

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:

Ursodeoxycholic acid (Ursofalk®) is recommended for use within NHS Wales for the treatment of hepatobiliary disorders associated with cystic fibrosis in children aged 1 month to 18 years.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies within five working days.

The Chairman confirmed the date of the next meeting on **Wednesday, 18th May 2016 in Cardiff** and closed proceedings.