

Enclosure No:	1/AWMSG/0217
Agenda Item No:	1 – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Draft minutes of the AWMSG meeting held Wednesday, 7th December 2016 commencing 9.30 am at the Park Inn, Cardiff North, CF23 9XF

VOTING MEMBERS PRESENT:

**Did not
participate in**

- | | | | |
|-----|--------------------|-----------------------------------------------|-----------|
| 1. | Dr Stuart Linton | Chair / Hospital Consultant | |
| 2. | Prof John Watkins | Vice-Chair / Public Health Wales | |
| 3. | Dr Anwen Cope | Healthcare professional eligible to prescribe | |
| 4. | Mrs Ellen Lanham | Community Pharmacist | |
| 5. | Prof Dyfrig Hughes | Health Economist | |
| 6. | Dr Sian Lewis | Welsh Health Specialised Services Committee | |
| 7. | Mrs Sue Murphy | Managed Sector Primary Care Pharmacist | |
| 8. | Mr Chris Palmer | Lay Member | |
| 9. | Mr Roger Williams | Managed Sector Secondary Care Pharmacist | |
| 10. | Dr Jeremy Black | General Practitioner | |
| 11. | Dr Emma Mason | Clinical Pharmacologist | |
| 12. | Mr Farhan Mughal | ABPI Cymru Wales | 5, 12, 13 |

IN ATTENDANCE:

Mr Scott Pegler, NMG Vice-Chair

Mrs Karen Samuels / Mr Tony Williams, Patient Access to Medicines Service, AWTTTC
Mrs Ruth Lang, Head of Liaison & Administration, AWTTTC

Ms Karan Edwards, Welsh Government

AWTTC APPRAISAL LEADS:

Dr Stephanie Francis
Dr Caron Jones
Ms Kelly Wood
Dr David Jarrom

AWTTC MEDICINES MANAGEMENT LEADS:

Ms Christine Collier
Ms Jessica Howells
Mrs Claire Thomas
Mr Richard Boldero

List of Abbreviations:

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

1. Welcome and introduction

The Chairman opened the meeting and welcomed members. The Chairman confirmed that the first three appraisals would be conducted in private as the submissions were associated with a Wales Patient Access Scheme. He confirmed the meeting would subsequently open to the public.

2. Apologies

Dr Cath Bale & Dr Sue Jeffs, Hospital Consultant
Dr Mark Walker & Dr Brendan Boylan, Medical Director
Dr Saad Al-Ismael, NMG Chair (Mr Scott Pegler deputising)
Mr Rob Thomas, ABPI Cymru Wales (Mr Farhan Mughal deputising)

3. Declarations of interest

Members were reminded to declare any interests. Mr Mughal declared a competitor interest in Appraisal 1 (fingolimod) and Appraisal 5 (adalimumab) as these medicines are, or may become, a competitor of a product developed, manufactured, sold or supplied by a company in which he has a current personal financial interest. The Chairman confirmed that Mr Mughal would not participate or vote in these appraisals.

4. Minutes of previous meeting

The minutes of the previous meeting were checked for accuracy. Dr Black asked that the second paragraph on page 12 be amended to read that the applicant company delegate is the "only UK employee". With that amendment the minutes were approved.

Mr Mughal left the meeting.

5. Appraisal 1: Full Submission (PAS)

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

The Chairman welcomed delegates from Novartis Pharmaceuticals 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 further interests were declared. The Chairman confirmed that only AWTTTC staff remained in the public gallery. The company delegates were reassured that proceedings would be confidential and the Chairman commenced with the appraisal.

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.

Dr Stephanie Francis, AWTTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR. She highlighted that fingolimod is available in NHS Scotland for the rapidly evolving severe patient population and is included in the NHS England commissioning policy for disease modifying therapies for patients with multiple sclerosis.

Mr Scott Pegler, NMG Vice Chair, confirmed that NMG had appraised Fingolimod (Gilenya®) on Wednesday, 2nd November and did not support use within NHS Wales as a single disease modifying therapy in highly active relapsing remitting multiple sclerosis for adult patients with

rapidly evolving severe relapsing remitting multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI. It was the view of NMG that the case for cost-effectiveness had not been proven as there were several uncertainties and limitations in the economic model provided in the company's submission; in particular there was uncertainty surrounding the proportion of patients retreated with the comparator, alemtuzumab (Lemtrada[®]) and therefore NMG were not convinced that fingolimod (Gilenya[®]) was cost-effective compared to alemtuzumab (Lemtrada[®]).

The Chairman confirmed the scope of the appraisal and reminded members that therapy in highly active relapsing remitting multiple sclerosis (MS) is covered by NICE TA254. He clarified the scope of the appraisal which only related to disease modifying therapy in highly active relapsing remitting MS in adults with rapidly evolving severe relapsing remitting multiple sclerosis. The Chairman invited members to seek clarification of any outstanding issues of clinical effectiveness. Clarification was sought in relation to disease progression and relapse rates. Members discussed the safety risks and the company delegate clarified the monitoring requirements in relation to the first dose. The company delegate elaborated on the reports of adverse reactions and stated that the rate of adherence was good due to it being an oral therapy. Attention was drawn to the MHRA safety alerts. There was discussion over patient preference and the company delegates informed members of a survey of 350 MS patients who were asked to rate their preference for attributes of therapy; oral therapy was identified as the most important factor. Members acknowledged that it had not been possible for the company to undertake an indirect comparison with alemtuzumab for the rapidly evolving severe patient population and the company delegates explained the challenges they faced in trying to demonstrate comparative clinical efficacy.

The Chairman referred to the summary of clinical expert views. Experts said that they would consider offering fingolimod to people with highly active multiple sclerosis who are unwilling to take the main treatment options, natalizumab or alemtuzumab, or for whom monoclonal antibody treatments are contraindicated. It was noted that one expert stated that the availability of fingolimod as a first-line therapy would align Wales with Europe and the rest of the world; and that fingolimod would offer a valuable oral alternative to existing therapies.

The Chairman invited Prof Dyfrig Hughes to comment on the case for cost-effectiveness. Prof Hughes confirmed his role as the AWMSG health economist and confirmed that he had no involvement in discussions at NMG or in the production of the ASAR. Prof Hughes summarised the key aspects of the case for cost-effectiveness as outlined in the ASAR and highlighted the limitations in the submission. He stated that the medicine appeared to be less effective but lower in cost. Prof Hughes then commented on the budget impact and summarised the key issues. The applicant company delegates thanked Professor Hughes for providing a good summary of the evidence and highlighted their justification for the approach they had taken, commenting that their estimate for retreatment rates for alemtuzumab was a conservative one. The Chairman acknowledged that the company had made an effort to explore various scenarios and explained that AWMSG takes a broader view than NMG.

The Chairman confirmed that two patient questionnaires had been received, one from the Multiple Sclerosis Society and one from the Multiple Sclerosis Trust, and asked Mr Palmer to relay the key issues from a patient perspective. Mr Palmer informed members of the benefits fingolimod offered to patients – a low annualised rate of relapse and a higher relapse free rate, lower risk of disability progression and a reduction in lesions to the brain. It might also help people with multiple sclerosis to remain in work and produce a positive impact on their lifestyle and that of their carers. The oral method of administration and convenience to patients was noted. The patient organisations also highlighted possible adverse reactions associated with fingolimod and the potential for slightly lower efficacy in terms of reduction in relapse rates compared to natalizumab and alemtuzumab.

Members sought clarification of the requirement for medical supervision of the first dose in a hospital or clinic to monitor heart rate and blood pressure and asked how this compared to other alternative treatments. It was acknowledged that in North Wales patients are often travelling to England for infusion which is often difficult and inconvenient. Mrs Murphy agreed that patients have been travelling to England for infusion but also highlighted that there are an increasing number of services now in place in North Wales to avoid patients having to travel to England. It was also noted that a home healthcare service could provide a more convenient option. The company delegates clarified the monitoring requirements and informed the group of on-going studies to collect quality of life and compliance data.

Prior to closing the discussion, the Chairman asked the company delegates if they wished to provide further comment or highlight any aspect of their submission. The delegates reiterated the convenience and patient preference of oral therapy, the potential cost savings to NHS Wales and equity across the UK and thanked AWMSG for the comprehensive discussion. 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:

Fingolimod (Gilenya[®]) is recommended as an option for use within NHS Wales for use as a single disease modifying therapy in highly active relapsing remitting multiple sclerosis for adult patients with rapidly evolving severe relapsing remitting multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI. This recommendation applies only in circumstances where the approved Patient Access Scheme (PAS) is utilised or where the list/contract price is equivalent or lower than the PAS price.

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

The Chairman confirmed that the final appraisal recommendation would be announced later in public. The applicant company delegates left the meeting.

Mr Murghan joined the meeting.

6. Appraisal 2: Instructed appraisal (WPAS)

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

The Chairman welcomed delegates from Basilea Pharmaceutica International 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 individuals in the public gallery were linked to AWTTTC or the applicant company. The company delegates were reassured and the Chairman opened appraisal proceedings.

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

to final NICE guidance should this be subsequently published.

The Chairman invited the AWTTTC Appraisal Lead to set the context of the appraisal and Dr Caron Jones highlighted the key aspects of the submission outlined in the ASAR. She relayed the view of the CHMP that new effective medicines for the treatment of complex fungal infections are needed. Dr Jones confirmed that the medicine is available in Scotland via HTA.

The Chairman invited Mr Scott Pegler to feed back the relevant issues identified in the preliminary appraisal. Mr Pegler confirmed that NMG had appraised isavuconazole (Cresemba[®]) on Wednesday, 2nd November and supported use within NHS Wales as an option for the treatment of invasive aspergillosis in adults and the treatment of mucormycosis in adult patients for whom amphotericin B is inappropriate. It was noted that this recommendation would 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. Mr Pegler relayed NMG's view that isavuconazole (Cresemba[®]) satisfied the AWMSG criteria for orphan status.

The Chairman confirmed that the criteria for appraising orphan and ultra-orphan medicines and medicines developed specifically for rare diseases had previously been circulated and asked members to highlight any outstanding issues of clinical effectiveness. The company delegates were asked to summarise the clinical advantages of the treatment and they stated that the medicine was easier to use and safer, with no requirement for therapeutic monitoring or dose adjustment. There was discussion in relation to adverse reactions, particularly septic shock.

The Chairman referred to the summary of clinical expert views and asked Dr Jones to relay the key issues. Dr Jones highlighted the unmet need. Experts stated that treating mucormycosis is particularly difficult and for patients for whom amphotericin B is inappropriate the only alternative is off licence use of posaconazole. Dr Jones informed members that experts would welcome another option for the treatment of invasive fungal infections.

The Chairman invited Professor Dyfrig Hughes to comment on the case for cost-effectiveness. Prof Hughes confirmed his role as the AWMSG health economist and explained he had not been involved in the preliminary appraisal by NMG or in the production of the ASAR. Prof Hughes summarised the key aspects of the case for cost-effectiveness as outlined in the ASAR and commented on the budget impact estimates. The cost savings were noted. Members sought clarification in relation to the patient numbers and estimates of uptake.

The Chairman reminded members that AWMSG's policy for appraising orphan and ultra-orphan medicines, and medicines developed specifically for rare diseases, would be applied to this appraisal and a wider judgement of the value of the medicine and societal aspects would be an important component. He confirmed that the policy had been tabled and asked members to remind themselves of the criteria to be taken into account. Mr Palmer confirmed that no patient organisation questionnaires had been received and listed the organisations that had been contacted. There were no wider societal issues of note.

The Chairman confirmed that no patient questionnaires had been received and asked Mr Palmer to inform members of the organisations contacted for input during the appraisal process. Members considered wider societal issues and recognised the importance of patient choice in relation to treatment.

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

Isavuconazole (Cresemba[®]) is recommended as an option for use within NHS Wales for the treatment of invasive aspergillosis in adults and the treatment of mucormycosis in adult patients for whom amphotericin B is inappropriate. 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.

7. Appraisal 3: Limited Submission (WPAS)

Ivacaftor (Kalydeco[®]) granules for the treatment of cystic fibrosis (CF) in children aged two to less than six years weighing less than 25 kg who have one of the following gating (class III) mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R

The Chairman welcomed representation from Vertex Pharmaceuticals Limited and confirmed that the appraisal would be undertaken in private. The Chairman confirmed that individuals in the public gallery were employees of AWTTTC. The Chairman opened appraisal proceedings and 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 reminded members that additional criteria should be taken into account for appraising this medicine and confirmed that AWMSG's policy for appraising orphan and ultra-orphan medicines, and medicines specifically for rare diseases, had been tabled.

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 for a limited submission 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 the right to request a full submission if the budget impact exceeded that estimated in the submission.

Ms Kelly Wood, the AWTTTC Appraisal Lead, set the context of the appraisal and summarised the ASAR. Ms Wood confirmed that the application was considered eligible for a limited submission based on it being a minor licence extension. It was noted that ivacaftor has designated European Medicines Agency orphan status.

Dr Pegler confirmed that NMG had appraised the medicine on Wednesday, 2nd November and supported use of ivacaftor (Kalydeco[®]) within NHS Wales as an option for the treatment of children with CF aged two years to less than six years and weighing less than 25 kg who have one of the following gating (class III) mutations in the CF transmembrane conductance regulator (CFTR) gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R. It was noted that the recommendation would 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 ivacaftor (Kalydeco®) satisfied the AWMSG criteria for ultra-orphan status.

The Chairman invited members to highlight any outstanding issues. There were none. The Chairman referred members to the summary of clinical expert views and asked Ms Wood to relay the salient issues. Experts stated that patients treated with ivacaftor demonstrated preservation of lung function compared to the natural history of deterioration commonly seen in patient receiving standard care. Experts are of the view that earlier initiation of ivacaftor treatment may lead to even greater long term survival. Clinical experts aim to commence all patients with CF and a G551D or other gating mutation within the license indication on ivacaftor from the age of two years. It was noted that the company estimates of patient numbers were consistent with expert opinion sought by AWTTTC. Experts also concurred with the standard of care treatments highlighted in the submission. The company delegate reassured members in relation to the accuracy of the CF data patient registry. Members acknowledged there would be an opportunity cost in extending the patient population and asked the company delegate to clarify real-world evidence of the impact on health outcomes.

The Chairman referred members to the patient organisation questionnaire from the CF Trust and asked Mr Palmer to relay the comments. Mr Palmer drew members' attention to the comment that, excluding lung transplant, ivacaftor is the only treatment that has the potential to preserve or restore lung function, slow the rate of decline and have a positive impact on life expectancy. This is considered by patients to be a 'step change' therapy and an opportunity to improve their quality of life and that of all the people who support them.

The Chairman asked the company delegates if they wished to comment or highlight any further points of discussion. The delegates thanked AWMSG for the questions and commented that the discussion had been good and interesting. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal.

Appraisal decision subsequently announced in public:

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

Ivacaftor (Kalydeco®) granules are recommended as an option for use within NHS Wales for the treatment of children with CF aged 2 years to less than 6 years and weighing less than 25 kg who have one of the following gating (class III) mutations in the CF transmembrane conductance regulator (CFTR) gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R. 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.

8. The meeting was opened to the public and the Chairman announced the recommendations pertinent to the three appraisals undertaken.

Chairman's report

The Chairman thanked those who had attended the AWMSG Masterclass held in Cardiff on 23rd November. The Chairman confirmed that the feedback had been very positive and the short film encouraging patient engagement in the AWMSG appraisal process had been

particularly well received. The Chairman reminded members of the Training Day scheduled on Wednesday 18th January for members and deputies of AWMSG and NMG and confirmed that two representatives from each health board's Medicines and Therapeutics Committee had been invited to attend.

The Chairman confirmed that the AWMSG Steering Committee met on 22nd November. The Committee received notes of the TDA Partnership Group meeting held on 25th October and the implementation report prepared by ABPI Cymru Wales. The Chairman reiterated the importance of timely implementation of AWMSG and NICE recommendations. The Chairman confirmed that the constitutions of AWPAG and NMG had been reviewed and updated. He invited members to submit comments to AWTTTC with regard to the NICE consultation on changes to technology appraisals and highly specialised technologies. Members were informed that due to the tight timelines, AWTTTC would compile a consultation response based on comments received from members of the Steering Committee and AWMSG. The Chairman confirmed that the Citizens Jury Report and minutes of the AWMSG meeting would be forwarded to the Antimicrobial Stewardship Group for their consideration.

The Chairman confirmed that representatives from AWTTTC had attended the Wales Access to Medicines Patient Charter Workshop held in Cardiff on Thursday, 17th November to talk about the implementation of recommendations following review of the IPFR process and also the One Wales process which enables interim decisions to be made for patient cohorts. AWTTTC gave a presentation on the AWMSG's process for appraising medicines, including orphan, ultra-orphan medicines and medicines developed specifically for rare diseases.

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

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

Levofloxacin (Quinsair[®]) is recommended as an option for restricted use within NHS Wales. Levofloxacin (Quinsair[®]) should be restricted for use as a third-line therapy in patients who do not respond to, or are intolerant of, second-line treatment with tobramycin for the management of chronic pulmonary infections due to *Pseudomonas aeruginosa* in adult patients with cystic fibrosis. Levofloxacin (Quinsair[®]) is not recommended for use within NHS Wales outside of this subpopulation. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

Sofosbuvir/velpatasvir (Epclusa[®]) is recommended as an option for use within NHS Wales for the treatment of chronic hepatitis C virus infection in adults. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent to or lower than the WPAS price.

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

Aviptadil/phentolamine (Invicorp®) is not recommended for use within NHS Wales for the symptomatic treatment of erectile dysfunction in adult males due to neurogenic, vasculogenic, psychogenic, or mixed aetiology.

The clinical and cost-effectiveness data presented in the submission were insufficient for AWMSG to recommend its use.

The following statement of advice have been ratified by Welsh Government, disseminated to the service and uploaded to the AWMSG website:

Abatacept (Orencia®) [AWTTC ref: 2985]

In the absence of a submission from the holder of the marketing authorisation, abatacept (Orencia®) cannot be endorsed for use within NHS Wales in combination with methotrexate for the treatment of highly active and progressive disease in adult patients with rheumatoid arthritis not previously treated with methotrexate.

Emtricitabine/tenofovir disoproxil fumarate (Truvada®) [AWTTC ref: 1625]

In the absence of a submission from the holder of the marketing authorisation, emtricitabine/tenofovir disoproxil fumarate (Truvada®) cannot be endorsed for use within NHS Wales for use in combination with safer sex practices for pre-exposure prophylaxis to reduce the risk of sexually acquired HIV 1 infection in adults at high risk

Lenvatinib (Kisplyx®) [AWTTC ref: 3290]

In the absence of a submission from the holder of the marketing authorisation, lenvatinib (Kisplyx®) cannot be endorsed for use within NHS Wales in combination with everolimus for the treatment of adult patients with advanced renal cell carcinoma following one prior vascular endothelial growth factor (VEGF)-targeted therapy.

Saxagliptin/dapagliflozin (Qtern®) [AWTTC ref: 2209]

In the absence of a submission from the holder of the marketing authorisation, saxagliptin/dapagliflozin (Qtern®) cannot be endorsed for use within NHS Wales for the treatment of adults aged 18 years and older with type 2 diabetes mellitus: to improve glycaemic control when metformin and/or sulphonylurea and one of the monocomponents of Qtern® do not provide adequate glycaemic control; when already being treated with the free combination of dapagliflozin and saxagliptin. This product is currently not marketed in the UK.

Thymidine kinase cell therapy (Zalmoxis®) [AWTTC ref: 2050]

In the absence of a submission from the holder of the marketing authorisation, thymidine kinase cell therapy (Zalmoxis®) cannot be endorsed for use within NHS Wales for use as an adjunctive treatment in haploidentical haematopoietic stem cell transplantation of adult patients with high-risk haematological malignancies

The Chairman announced the appraisals scheduled for the next meeting on Wednesday, 15th February 2017 in Cardiff:

Full Submission (PAS)

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

Applicant Company: Bayer Healthcare Pharmaceuticals

Limited Submission

Triptorelin (Decapeptyl® SR) as adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer. Also as neoadjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer.

Applicant Company: Ipsen Ltd

Instructed to appraise by Welsh Government
Vismodegib (Erivedge[®]) for the treatment of adult patients with symptomatic metastatic basal cell carcinoma, or locally advanced basal cell carcinoma inappropriate for surgery or radiotherapy
Applicant Company: Roche Products Ltd

Full submission - appraisal post CAPIG meeting
Human alpha1-proteinase inhibitor (Respreeza[®]) for maintenance treatment, to slow the progression of emphysema in adults with documented severe alpha1-proteinase inhibitor deficiency
Applicant Company: CSL Behring UK Ltd

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

9. Educational Pack: Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales

The Chairman invited Mrs Claire Thomas and Miss Chrissie Collier from AWTTTC to present Enclosure 5 – an updated educational pack to support the appropriate prescribing of hypnotics and anxiolytics across Wales. Mrs Thomas provided the background and an overview of the paper and explained that this was an update to the pack that was originally endorsed by AWMSG in 2011. Members were informed that the resource pack would provide key health professionals with a practical approach for the initiation and review of hypnotic and anxiolytic prescribing including examples of support material which can be used or adapted for this purpose. Mrs Thomas highlighted that WAPSU received requests for the previous version of the pack from all over the UK, and that it was known to be widely used across Wales. Mrs Thomas sought the endorsement of AWMSG and the Chairman opened the discussion. Members welcomed the updated document. There was unanimous support and agreement that the educational pack offered a valuable resource to primary care and members were keen to ensure that it had maximum impact at launch. Members discussed potential implementation plans. Dr Mason asked whether a similar document aimed at secondary care could be developed. Mrs Lanham suggested that community pharmacy could have a supportive role. Miss Collier and Mrs Thomas confirmed that the document had largely been used by prescribing advisers in GP practices to reduce prescribing of hypnotics and anxiolytics. Professor Watkins suggested a media campaign to achieve as wide an audience as possible. Mrs Thomas agreed to take the comments back to AWTTTC for consideration. The Chairman thanked members for their contributions to the discussion and confirmed AWMSG's endorsement.

10. Therapeutic Priorities and Clinical Effectiveness Prescribing Programme Summary 2017–2018

Mrs Claire Thomas and Mr Richard Boldero of AWTTTC presented the Therapeutic Priorities and Clinical Effectiveness Prescribing Programme Summary 2017–2018 and sought the endorsement of AWMSG. Mrs Thomas explained that the document aims to assist health boards in the development of the Clinical Effectiveness Prescribing Programmes, formally known as prescribing incentive schemes. In addition, the document signposts to resources that can be used as part of the General Medical Services (GMS) contract, Quality and Outcomes Framework (QOF) Medicines Management Indicator. The document is produced on an annual basis and has been updated for 2017–2018, and reformatted with the intention of making it more user friendly. The Chairman opened discussion and Professor Watkins asked whether the form of words in the table on page 5 under the target column should be reworded. Mrs Sue Murphy queried why the total antibacterial items indicator was not included in the National Outcomes Framework as a performance measure. It was noted that the performance measures are set by the Welsh Government and monitored on a quarterly basis. Mrs Thomas clarified that the National Prescribing Indicators for 2017-2018 had not been formally approved yet and

would be presented to AWMSG in February 2017. The Chairman confirmed AWMSG's support of this initiative and closed discussion.

11. **Dry Eye Syndrome**

Mr Boldero and Ms Jessica Howells from AWTTTC presented Enclosure 7 and asked members to consider the Dry Eye Syndrome Guidance document for endorsement. Mr Boldero explained the background and informed members that development of guidance had been at the request of the Chief Optometric Officer for Wales. It was noted that the cost of dry eye syndrome treatments for NHS Wales is approximately £3.4 million annually and, although some health boards had developed guidance, a more consistent and prudent approach to prescribing and the provision of self-care advice was required. The guidance aims to provide information to healthcare professionals so that they can better inform patients on how to manage their condition, aid healthcare professionals in prescribing and reduce spend on dry eye products.

Mr Boldero explained that the guidance would be used by healthcare professionals in a primary or secondary care setting, including pharmacists, optometrists, GPs, ophthalmologists and other hospital doctors (such as rheumatologists) and could be adapted by health boards in line with local requirements. Mrs Lanham asked whether a mechanism could be established for dissemination to community pharmacy. Members discussed the identification of an accredited list of optometrists. The Chairman confirmed AWMSG's support for the guidance and closed discussion.

12. **Appraisal 4 – Full Submission**

Ferric maltol (Feracru®) for the treatment of iron deficiency anaemia in adults with inflammatory bowel disease

The Chairman welcomed delegates from Shield Therapeutics. 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.

Dr Caron Jones, AWTTTC appraisal lead, set the context of the appraisal and highlighted the key aspects of the submission outlined in the ASAR. Dr Jones confirmed that the applicant company had requested that AWMSG consider the use of ferric maltol in a subpopulation of patients with mild to moderate iron deficiency anaemia that have failed on therapy with oral ferrous iron preparations.

Mr Pegler confirmed that NMG had appraised ferric maltol (Feracru®) on 2nd November and did not support its use within NHS Wales for the treatment of iron deficiency anaemia in adults with inflammatory bowel disease. NMG considered that the cost-effectiveness data presented in the submission were insufficient for NMG to recommend its use. Mr Pegler explained that the company's submission was based on a cost minimisation analysis; this may be acceptable, but only in circumstances where clinical equivalence is demonstrated in relation to a comparator. In line with AWMSG guidance, NMG considered the evidence presented did not support the case that ferric maltol and the comparator were therapeutically equivalent.

The Chairman asked members to highlight any outstanding issues of clinical effectiveness. Members sought clarification in relation to the inclusion/exclusion criteria in relation to the AEGIS trial and asked the company delegates to comment on the drop-out rate. The company

delegates acknowledged that the dataset is limited and provided the rationale in relation to their submission. The safety profile was noted.

The Chairman referred members to the summary of clinical expert views and Dr Jones highlighted the key issues. Experts stated that for patients who are intolerant to oral iron preparations, intravenous iron formulations are effective at correcting iron deficiency anaemia in inflammatory bowel disease. It was highlighted that in some patients there is a risk of serious allergic reaction with the administration of intravenous iron. Experts stated that treatment with intravenous iron is associated with resource implications as it is administered in day care units which require intensive nursing and pharmacy input. It was the view of clinical experts that a safe and effective oral iron formulation for use in patients with inflammatory bowel disease would reduce the impact on health resources and patient time.

The Chairman invited Professor Hughes to comment on the case for cost-effectiveness. Prof Hughes confirmed his role as the AWMSG health economist and confirmed that he had not been involved in the New Medicines Group's preliminary appraisal or in the production of the ASAR. Prof Hughes summarised the key aspects of the case for cost-effectiveness as outlined in the ASAR and highlighted the limitations of the evidence provided. He commented on the budget impact estimates and stated his view that equivalence in efficacy is an assumption. The company delegates acknowledged this and explained that they had taken a conservative approach to ensure they had a robust model given the level of uncertainties. The company delegates justified their choice of a cost minimisation analysis and explained what had been done to address some of the uncertainties.

The Chairman asked Mr Palmer to highlight the salient points from the patient organisation questionnaire that had been submitted by Crohn's and Colitis UK and made available to members for their consideration. Mr Palmer relayed the view of patients that ferric maltol would offer an alternative treatment option and may minimise the side effects which are often experienced with intravenous iron medication; it would improve the distressing symptoms of the disease and allow patients more control and less disruption of their daily lives.

The Chairman thanked the company delegates for the professional discussion and asked if they wished to comment or highlight any further issues. They explained the approach being taken to introduce the medicine in England and confirmed their appreciation of the discussion and openness of the 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. 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:

Ferric maltol (Feraccru[®]) is not recommended for use within NHS Wales for the treatment of iron deficiency anaemia in adults with inflammatory bowel disease. The cost-effectiveness data presented in the submission were insufficient for AWMSG to recommend its use.

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

Mr Murghan left the meeting.

13. **Appraisal 5: Limited submission**

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

The Chairman confirmed that there would be no representation from Abbvie Limited.

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No further 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 informed members that the application had been considered eligible for a limited submission and no cost-effectiveness information is required. He confirmed that for a limited submission 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 the right to request a full submission if the budget impact exceeded that estimated in the submission.

Dr David Jarrom, the AWTTTC appraisal lead, set the context of the appraisal and provided an overview of the evidence, as summarised in the ASAR. Dr Jarrom confirmed that the application had been considered appropriate for a limited submission as it was a minor licence extension to a medicine that had previously been appraised and recommended for use by AWMSG and there would be minimal budget impact. Dr Jarrom confirmed that clinical experts in Wales had agreed with the applicant company that off-label infliximab would be the most appropriate comparator.

Mr Pegler confirmed that NMG had appraised the medicine on Wednesday, 2nd November and had supported the use of adalimumab (Humira®) as an option for use within NHS Wales for the treatment of moderately to severely active Crohn's disease in paediatric patients (from 6 years of age) who have had an inadequate response to conventional therapy including primary nutrition therapy and a corticosteroid and/or an immunomodulator, or who are intolerant to or have contraindications for such therapies.

The Chairman asked members if they had any outstanding issues; however, there was no representation from the applicant company to respond to members' questions. The Chairman referred members to the summary of clinical expert views. It was noted that experts envisaged that adalimumab, as the licensed option, would be used as primary biological therapy within the indication for patients and would be of particular value where there are issues with venous access (phobia of needles or difficult venous access), hospital attendance, or reduced/loss of response to infliximab following development of anti-infliximab antibodies.

The Chairman asked Mr Palmer to highlight the salient points from the patient organisation questionnaire that had been submitted by Crohn's and Colitis UK. Mr Palmer relayed the view that access to this licensed medicine is crucial as it will provide an alternative treatment option. It will alleviate the distress and disruption to family life and education and is likely to have a profound psychological positive impact on the child and his or her carers/parents. The treatment can be given at home which would allow greater freedom from regular hospital visits.

There were no other issues of note and 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:

Adalimumab (Humira®) is recommended as an option for use within NHS Wales for the treatment of moderately to severely active Crohn's disease in paediatric patients (from 6 years of age) who have had an inadequate response to conventional therapy including primary nutrition therapy and a corticosteroid and/or an immunomodulator, or who are intolerant to or have contraindications for such therapies.

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 wished everyone a Merry Christmas and closed the meeting.

Date of next meeting – Wednesday, 15th February 2017 in Cardiff