Enclosure No:	**1/AWMSG/0317**
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, 15th February 2017 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	1-4
3.	Dr Cath Bale	Hospital Consultant	
4.	Dr Anwen Cope	Healthcare professional eligible to prescribe	
5.	Mr Stuart Davies	Finance Director	1-4
6.	Mrs Ellen Lanham	Community Pharmacist	
7.	Ms Pippa Anderson	Health Economist	
8.	Dr Sian Lewis	Welsh Health Specialised Services Committee	
9.	Mrs Sue Murphy	Managed Sector Primary Care Pharmacist	13-14
10.	Mr Chris Palmer	Lay Member	
11.	Mr John Terry	Managed Sector Secondary Care Pharmacist	
12.	Dr Jeremy Black	General Practitioner	
13.	Dr Balwinder Bajaj	Clinical Pharmacologist	
14.	Dr Mark Walker	Medical Director	13-14

IN ATTENDANCE:
Dr Saad Al-Ismail, NMG Chair
Mrs Karen Samuels, Head of PAMS, AWTTC
Mrs Ruth Lang, Head of Liaison & Administration, AWTTC
Ms Kath Haines, Head of WAPSU, AWTTC
Dr Robert Bracchi, CAPIG Chairman

AWTTC Leads:
Dr Stephanie Francis, Senior Scientist
Mrs Claire Ganderton, Senior Pharmacist
Mrs Claire Thomas, Senior Pharmacist
Mr Richard Boldero, Senior Pharmacist

There was no representation from Welsh Government

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 opened the meeting and welcomed members. The Chairman confirmed that the first appraisal would be conducted in private as the submission included a confidential Department of Health Patient Access Scheme. He confirmed the meeting would subsequently open to the public.

2. Apologies

Dr Emma Mason (Dr Balwinder Bajaj deputising)
Professor Dyfrig Hughes (Ms Pippa Anderson deputising)
Mrs Louise Williams and Mrs Mandy James (Senior Nurse)
Mr Bill Malcolm (ABPI Cymru Wales)

3. Declarations of interest

Members were reminded to declare any interests. No interests were declared.

4. Minutes of previous meeting

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

5. Appraisal 1: Full Submission (PAS)

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

The Chairman welcomed delegates from Bayer plc. The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No further interests were declared. Having confirmed that only AWTTC staff remained in the public gallery the Chairman commenced 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.

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 members will focus on the budget impact and wider societal issues.

The Chairman confirmed that the company delegates would be asked to leave the meeting for a short period to enable confidential discussion in relation to the comparator medicine, which also had an associated Patient Access Scheme.

Mrs Claire Ganderton, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the submission outlined in the ASAR. It was noted that the medicine is available in NHS Scotland for this indication.

Dr Al-Ismail confirmed that NMG had appraised aflibercept (Eylea®) on 11th January 2017 and supported use as an option within NHS Wales for the treatment of adult patients with visual impairment due to myopic choroidal neovascularisation. It was the view of NMG that this recommendation should apply 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 invited discussion in relation to the case for clinical effectiveness. Clarification

was sought in relation to the adverse effects and consequences of these for patients. The company delegates reassured members that the adverse effect profile was similar to that of the comparator medicine, that there were no new safety signals for aflibercept and confirmed the CHMP monitoring requirements. There was discussion around how improvement in EQ5D scores impacted on the quality of life of the patient and how the letter gain seen in the pivotal study would impact on a patients' day-to-day living.

The Chairman referred to the summary of clinical expert views. Experts stated that ranibizumab (Lucentis®) is the predominant treatment option in Wales; however, aflibercept would be a useful option for specialist only prescribing. It was the view of experts that the disease responds well to treatment and they were not aware of any unmet need in this area.

The Chairman invited Ms Pippa Anderson to comment on the case for cost effectiveness. Ms Anderson confirmed her role as the AWMSG health economist and confirmed that she had no involvement in discussions at NMG or in the production of the ASAR. Ms Anderson summarised the key aspects of the case for cost effectiveness as outlined in the ASAR and highlighted the limitations of the cost-minimisation analysis (CMA) presented to AWMSG. The company delegates responded by explaining their rationale for submitting a CMA and explained why neither a CMA nor cost-utility analysis (CUA) would have been ideal. They considered their approach provided a transparent and conservative analysis. Clarification was sought in relation to the injection frequency and the number of patients estimated to be treated. Members also touched on the wider societal issue of eye service clinic capacity within NHS Wales.

The company delegates left the meeting for a short period to enable AWMSG to discuss the cost effectiveness and budget impact in relation to the comparator medicine in private. On their return, the Chairman moved onto the views of patients. It was confirmed that the Macular Society had sought comments from an individual patient living in England who had experience of using the medicine. Mr Palmer relayed the key issues from a patient perspective. He pointed out that less frequent injections would have a beneficial impact on patients and reiterated the importance of having a range of treatment options available to clinicians and patients. The Chairman then asked members if there were any outstanding wider societal issues members wished to discuss; none were raised.

Prior to closing the discussion, the Chairman referred to the comprehensive response from the marketing authorisation holder and asked the company delegates if they wished to provide further comment or highlight any aspect of their submission. The delegates reiterated the reasons for their choice of approach.

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 and members retired to vote in private.

Subsequent to the vote, the meeting was opened to the public and the Chairman announced the appraisal recommendation:
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:

Aflibercept (Eylea®) is recommended as an option for use within NHS Wales for the treatment of adult patients with visual impairment due to myopic choroidal neovascularisation. 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.

6. Chairman's report (verbal update)

The Chairman welcomed the Cabinet Minister's announcement of 10th January that the new treatment fund had opened for business. Members were informed that the fund would provide £16 million annually to support health boards speed up the implementation of medicines recommended for use by NICE and AWMSG.

The Chairman confirmed that positive feedback had been received in relation to the AWMSG Training Day held in Cardiff on Wednesday, 18th January and thanked members for attending. The Chairman thanked AWTTC staff involved in the organisation of this event and speakers for their contributions.

The Chairman confirmed that a response by AWMSG to the NICE consultation on changes to technology appraisals and highly specialised technologies had been submitted within the deadline.

The Chairman informed members that the AWMSG Steering Committee had met on 24th January. He stated that final NICE HST advice is anticipated in relation to migalastat (Galafold) for the treatment of Fabry disease in people over 16 years of age with an amenable mutation. He confirmed that no barriers to its implementation had been highlighted by WHSSC and confirmed AWMSG's recommendation to the Cabinet Secretary would be to accept NICE HST advice on the publication of this advice.

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

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 the following adult patient group:

- 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.

Ivacaftor (Kalydeco®) granules are recommended as an option for use within NHS Wales for the treatment of children with cystic fibrosis (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.

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.

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.

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

Crizotinib (Xalkori®) AWTTC ref: 3207
In the absence of a submission from the holder of the marketing authorisation, crizotinib (Xalkori®) cannot be endorsed for use within NHS Wales for the treatment of adults with ROS1-positive advanced non-small cell lung cancer.

Glycopyrronium bromide AWTTC ref: 3348
In the absence of a submission from the holder of the marketing authorisation, glycopyrronium bromide cannot be endorsed for use within NHS Wales in adults as an add-on therapy in the treatment of peptic ulcer.

Human normal immunoglobulin (Octagam 5%®) AWTTC ref: 3368
In the absence of a submission from the holder of the marketing authorisation, human normal immunoglobulin (Octagam 5%®) cannot be endorsed for use within NHS Wales for the treatment of chronic inflammatory demyelinating polyneuropathy in adults, and children and adolescents (0–18 years).

Idelalisib (Zydelig®) AWTTC ref: 2375
In the absence of a submission from the holder of the marketing authorisation, idelalisib (Zydelig®) cannot be endorsed for use within NHS Wales in combination with an anti-CD20 monoclonal antibody (ofatumumab) for the treatment of adult patients with chronic lymphocytic leukaemia; who have received at least one prior therapy, or as a first-line treatment in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy.

The Chairman informed members that following a negative appraisal by NMG of 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, the marketing authorisation holder has requested a meeting of the Clinician and Patient Involvement Group (CAPIG) prior to appraisal by AWMSG. It was confirmed that the appraisal process had been suspended.

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

Appraisal 1: Full Submission (WPAS)
Bevacizumab (Avastin) in combination with paclitaxel and cisplatin or, alternatively, paclitaxel and topotecan in patients who cannot receive platinum therapy, for the treatment of adult patients with persistent, recurrent, or metastatic carcinoma of the cervix
Applicant Company: Roche Products Ltd

Appraisal 2: Full Submission (PAS)
Idelalisib (Zydelig) as monotherapy for the treatment of adult patients with follicular lymphoma (FL) that is refractory to two prior lines of treatment
Applicant Company: Gilead Sciences Ltd

Appraisal 3: Full Submission (WPAS)
Ivacaftor (Kalydeco) for the treatment of patients with cystic fibrosis (CF) aged 18 years and older who have an R117H mutation in the CFTR gene
Applicant Company: Vertex Pharmaceuticals 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.

The Chairman asked members to sign and return the confidentiality statement to AWTTC.

7. Feedback from AWPAG Meeting held 14th December 2016

Ms Kath Haines presented Enc 3/AWMSG/0217, the draft minutes of the AWPAG meeting held in December 2016. Members queried why the shared care guidance for the treatment of gender dysphoria in transwomen had not included transmen. Ms Haines agreed to seek clarification from Welsh Government. Dr Black referred to a protocol from Exeter which was aimed at GPs which covered transgender men and women. Mrs Haines confirmed that Mr Tim Banner would be attending the next AWPAG meeting for the development of guidance for nurses and care home providers in respect of medicines administration and support workers, and to progress work on the equitable and consistent approach to domiciliary care medicines administration across Wales. Mrs Murphy asked why the NOAC alert card project had not progressed. Ms Haines confirmed that AWMSG's comments had been fed back to the Quality and Safety Sub-Committee of the All Wales Chief Pharmacists Group who felt that development of a NOAC alert card should not be currently progressed on an All Wales basis. Mrs Murphy stated that a Welsh-specific card is needed within Wales and she would follow this up outside of the meeting. The Chairman closed discussion and thanked AWPAG for developing the work of AWMSG.

8. National Prescribing Indicators 2016–2017 – Analysis of Prescribing Data to September 2016

Mr Richard Boldero and Mrs Claire Thomas presented an analysis of the National Prescribing Indicators, for the second quarter of 2016–2017, to AWMSG for information. For the current year, 13 primary care NPIs focus on seven therapeutic areas and the reporting of adverse reactions to medicines via the Yellow Card Scheme, in addition to 3 NPIs for secondary care. Members were informed that the paper is pertinent to the 'Improving Health – Prescribing Guidance' recommendation in the AWMSG Five-year Strategy 2013–2018: *AWMSG will work with health boards and other stakeholders to promote the safe, effective and cost-effective use of medicines in Wales.* Mrs Thomas highlighted that there had been improvements across Wales, in line with the aims of the indicators, for 10 of the 12 primary care NPIs with a threshold, compared with the equivalent quarter of the previous year. The two indicators which did not show an improvement were PPI prescribing, which had increased by 0.51%, and gabapentin and pregabalin prescribing, which had increased by 13.8%. The NPIs associated with the greatest improvements were co-amoxiclav, cephalosporins and hypnotics and anxiolytics, which all demonstrated reductions.

Mr Boldero presented the analysis for the secondary care NPIs. The antibiotic surgical prophylaxis indicator value was the same as in the previous quarter of 2016-2017, at 14%. For the insulin prescribing and prescribing of biosimilars NPIs the quarter for comparison was the equivalent quarter of 2015-2016. In primary care there was a decrease of 0.33% in the use of long-acting insulin analogues, with a 1.96% increase in secondary care. For the prescribing of

biosimilars NPI there was an increase in the use of the filgrastim biosimilars from 98.4% to 98.8%, and for infliximab biosimilar use there was an increase from 12.8% to 46.1%, in keeping with the aim of the NPI.

The Chairman opened discussion and there was debate over the two indicators that had not shown an improvement – PPIs and gabapentin and pregabalin. Members asked whether health boards would be asked to respond to this information. There was general agreement that implementation and prioritisation of the national prescribing indications differed across health boards. Mrs Haines confirmed that a day for sharing best practice had been arranged for 28th June 2017 and AWPAG would be discussing the programme at their next meeting. Members suggested that IT would play an important role in changing behaviour and there was discussion over Scriptswitch and similar electronic systems that would offer a trigger tool for prescribing behavioural change. The Chairman welcomed the sharing of best practice and closed discussion.

9. National Prescribing Indicators 2017–2018

Mr Boldero and Mrs Claire Thomas presented Enclosure 5 and asked AWMSG to endorse the NPIs proposed for 2017-2018. Mrs Thomas explained the process for developing the indicators and thanked consultees. The key changes were highlighted - the introduction of two new NPIs to be monitored by Audit+ (the anticholinergic effect on cognition and NSAIDs in CKD), the introduction of a new opioid patch NPI to be monitored via CASPA and a change of inhaled corticosteroid (ICS) NPI measure from low-strength to high-strength ICS items as a percentage of all ICS prescribing. Members were informed of the retirement of two NPIs; lipid-regulating drugs (items of bile acid sequestrants, fibrates, nicotinic acid and omega-3 fatty acid compounds as a percentage of total lipid-regulating items) and NSAIDS (ibuprofen and naproxen as a percentage of all NSAID prescribing). The change of title for the antibiotic indicators to 'Antimicrobial Stewardship' was noted.

Mr Boldero explained that due to this being the first year for the secondary care NPIs there was still time needed for these to embed into practice before the optimum benefit will be realised. Therefore the AWPAG Task and Finish group had decided to keep the secondary care NPIs the same for 2017-2018 as for 2016-2017.

The Chairman opened discussion and Dr Cope asked whether dental prescribing of antibiotics could be considered for inclusion in the 2018-2019 NPIs. The opportunity to link with Audit+ was welcomed by members. It was noted that England have combined the co-amoxiclav, cephalosporin and quinolone indicators, however Mrs Thomas confirmed that the indicator sub-group had considered but dismissed this for Wales for 2017-2018.

10. National Prescribing Indicators 2017–2018 Supporting Information for Prescribers

Mrs Thomas asked members to endorse the NPI supporting information document which has been streamlined from previous years, and contains information for both primary and secondary care NPIs. Mrs Thomas noted that AWPAG members welcomed the succinct document and noted that should prescribers require further information, they could refer to the main document which includes a more detailed description of each of the indicators. Dr Black considered the resource would be very useful for GPs with a prescribing interest. Mrs Thomas confirmed that the supporting information would be disseminated widely and made available for all prescribers.

The Chairman thanked AWPAG for developing the NPIs and concise supporting information and closed discussion.

11. Appraisal 2: Full Submission

Human alpha1-proteinase inhibitor (Respreeza®) for maintenance treatment, to slow the progression of emphysema in adults with documented severe alpha1-proteinase inhibitor deficiency (e.g. genotypes PiZZ, PiZ(null), Pi(null,null), PiSZ). Patients are to be under optimal

pharmacologic and non-pharmacologic treatment and show evidence of progressive lung disease (e.g. lower forced expiratory volume per second [FEV1] predicted, impaired walking capacity or increased number of exacerbations) as evaluated by a healthcare professional experienced in the treatment of alpha1-proteinase inhibitor deficiency.

The Chairman welcomed delegates from CSL Behring 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 reminded members that additional criteria for appraising a medicine developed specifically to treat a rare disease should be applied when appraising this medicine. AWMSG's policy for appraising orphan and ultra-orphan medicines, and medicines developed specifically for rare diseases was tabled.

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 members will focus on the budget impact and wider societal issues.

Mrs Claire Ganderton, AWTTC appraisal lead, set the context of the appraisal and highlighted the key aspects of the submission outlined in the ASAR. Mrs Ganderton informed members that human alpha1-proteinase inhibitor (Respreeza®) is the first medicine licensed in the UK specifically for the treatment of this condition. The medicine is not currently available within NHS Scotland or NHS England.

Dr Al-Ismail confirmed that NMG had appraised human alpha1-proteinase inhibitor (Respreeza®) on 5th October 2016 and had not supported its use within NHS Wales. It was the view of NMG that the applicant company had not presented sufficiently robust clinical and economic analyses to gain approval by NMG. It was noted that NMG considered that human alpha1-proteinase inhibitor (Respreeza®) satisfied the AWMSG criteria for a medicine developed specifically to treat a rare disease.

The Chairman asked members to highlight any outstanding issues of clinical effectiveness. Members sought clarification in relation to the use of lung density decline as the primary endpoint measure in the pivotal study and how this translates into clinical effect. The company delegate explained that it is not feasible to recruit sufficient numbers of patients into a study when using traditional outcome measures and referred to data from patients in other countries treated with human alpha1-proteinase inhibitor. There was further discussion on the relationship between lung density and other health outcome measures and the company highlighted correlations with FEV1 and mortality from published and registry data. A suggestion was made to the company that it might be beneficial for them to collect quality of life data from around the world, particularly if there was an intention to submit for appraisal by NICE. There was discussion over the definition of rapidly declining lung function and the company confirmed that there were no specific criteria and patients needing treatment would be identified by clinicians with expertise in managing patients with alpha1-proteinase inhibitor associated emphysema. The company was asked to clarify the measure of non-response and the

company confirmed that in terms of lung density measurements non-response has not been seen. AWMSG members asked what clinical improvements could be expected over the first two, three or five years following treatment initiation; the company explained that there would be no such data because the disease progresses slowly and it would take many more years for clinical improvements to be seen.

The Chairman referred members to the summary of clinical expert views and Mrs Ganderton highlighted the key issues and confirmed that the number of patients eligible for treatment in Wales is expected to be around 30. Mrs Ganderton also confirmed that the use of lung density decline as the primary endpoint was supported by the clinical expert in attendance at NMG. Clinical experts confirmed that Welsh patients can be referred to a specialist centre in England for assessment, monitoring and treatment. The closest specialist Centre to Wales is in Birmingham and any treatments recommended by the specialist centre are prescribed locally. One expert stated that access to augmentation therapy in Wales would be a step changing improvement for the management of alpha1-proteinase inhibitor deficiency-related emphysema because this would be the first time that patients living in Wales would be able to receive a treatment that would modify their disease and reduce the rate of emphysema progression. According to all experts, the need for specialist alpha1-proteinase inhibitor deficiency services in Wales is currently unmet and there is inequity in the availability of intravenous augmentation therapy for UK patients compared with those in Europe, the USA and Canada.

The Chairman invited Ms Pippa Anderson to comment on the case for cost-effectiveness. Ms Anderson confirmed her role as the AWMSG health economist and confirmed that she had not been involved in the New Medicines Group's preliminary appraisal or in the production of the ASAR. Ms Anderson summarised the key aspects of the case for cost-effectiveness as outlined in the ASAR and highlighted the limitations of the evidence provided. She welcomed the transparent and clear methodological approach and drew attention to the high level of uncertainty in the cost-effectiveness. She acknowledged the rarity of the disease and made the point that NMG's decision not to support use within NHS Wales would have been driven overwhelmingly by the acquisition cost of the medicine. The Chairman reminded members that AWMSG's policy for appraising rare medicines had been developed specifically for occasions where the evidence-base is challenging. The company delegate responded by justifying the high cost of the medicine because it is a human product. The Chairman referred members to the budget impact estimates in Table 4 of the ASAR.

The Chairman explained the purpose of CAPIG and invited Dr Rob Bracchi, as CAPIG Chairman, to provide a summary of the CAPIG meeting held on 2nd December 2016. Dr Bracchi informed members that the meeting had been attended by representatives of the patient organisation, clinical experts, the Community Health Council and the applicant company. Dr Bracchi explained the symptoms of the disease and stated that current treatments do not correct the root cause, the deficiency of alpha1-proteinase inhibitor. He highlighted the lack of a specialist centre in Wales with access to pulmonary and hepatology services. Dr Bracchi informed members that case reports had been received in which patients reported significant benefits in activity levels, improvements in quality of life and independence, ability to stay in employment for longer, and the ability to participate fully in family, social and community life. He made the point that Respreeza® offered hope to patients and their families, and reassurance that they are receiving a treatment that treats the underlying deficiency.

The Chairman asked Mr Palmer to address the Group. Mr Palmer confirmed that he had been in attendance at the CAPIG meeting where a patient had read out her story which he had found very emotional. He read extracts of the story which highlighted the impact of the disorder on the patient. Mr Palmer informed members that several other patient stories had been forwarded on to him after the CAPIG meeting and he relayed the key points, including the ability to work for the patient and carer, the cost of care, the relatively young age of patients, the impact and burden on the family and that lung transplantation is seen as the last resort for patients. The Chairman confirmed that members had all received and read the patient

organisation questionnaire from Alpha-1 UK Support Group, the patient relative and three individual patients.

The Chairman then asked members if there were any outstanding wider societal issues members wished to discuss; none were raised.

Prior to closing the discussion, the Chairman referred to the comprehensive response from the marketing authorisation holder and asked the company delegates if they wished to provide further comment or highlight any aspect of their submission. The delegates reiterated that preserving lung tissue, as demonstrated in the pivotal study, is innately good and that they had put the best case forward that they could.

In concluding, the Chairman thanked the company delegates. 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:

Human alpha1-proteinase inhibitor (Respreeza®) is not recommended for use within NHS Wales for maintenance treatment, to slow the progression of emphysema in adults with documented severe alpha1-proteinase inhibitor deficiency (e.g. genotypes PiZZ, PiZ(null), Pi(null,null), PiSZ). The case for clinical effectiveness 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.

12. Appraisal 3: Limited Submission

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

The Chairman welcomed representation from Ipsen Limited (via J B Medical Ltd).

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 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 Stephanie Francis, the AWTTC Appraisal Lead, set the context of the appraisal and summarised the ASAR. She confirmed that the application had been considered eligible for a limited submission as the licence extension is considered minor and the anticipated usage in NHS Wales is considered to be of minimal budgetary impact.

Dr Al-Ismail confirmed that NMG had appraised the medicine on Wednesday, 11th January 2017 and had supported use of triptorelin (Decapeptyl® SR) for this indication as an option.

The Chairman opened discussion and no issues relating to the case for clinical-effectiveness were raised. Clarification was sought in relation to the increased rate of cardiovascular events and needle thickness. The company delegate confirmed that training and support is offered by the company to nurses. The Chairman referred members to the summary of clinical expert views and Dr Francis relayed the experts' views that neoadjuvant and adjuvant hormone therapy with radiotherapy was the standard treatment for prostate cancer. The view expressed was that triptorelin does not have any particular advantages over existing therapies and prescribing should be based on local convenience and cost.

The Chairman referred members to the two patient organisation questionnaires and, for the purposes of transparency, asked Mr Palmer to highlight any salient issues. Mr Palmer referred to comments received from the West Wales Prostate Cancer Support Group and Prostate Cancer UK. Mr Palmer relayed the view that an additional treatment option would be helpful and that triptorelin may suit some patients better than others. It was felt that an initial one month injection would seem a sensible option for new patients whom require hormone therapy drug given the possibility of an adverse reaction. The patient information leaflet was considered by the West Wales Prostate Cancer Support Group to be very helpful. Prostate Cancer UK made the point that some patients would prefer six-monthly injections compared to one or three monthly injections. Mr Palmer reiterated the importance of having a choice of treatment options for patients and their clinicians.

The Chairman asked the company delegates if they wished to comment or highlight any further points of 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:

Triptorelin (Decapeptyl® SR) is recommended as an option for use within NHS Wales as an adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer and as neoadjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer.

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 Mark Walker and Mrs Sue Murphy left the meeting.

13 Medicines Management Resource for Chronic Kidney Disease

14 CEPP National Audit: Medicines Management for Chronic Kidney Disease

The Chairman asked Mr Boldero to present these two documents which complement and support each other.

Mr Richard Boldero, AWTTC Lead, presented an overview of the development of the medicines management resource for chronic kidney disease (CKD) and CEPP audit. He explained that the documents are intended to improve the identification of patients and their management and therapeutic outcomes within primary care. Mr Boldero stated that the consultation had received a number of responses which had been incorporated into the documentation. Ms Haines confirmed that AWTTC had liaised closely with renal colleagues in the development of this work. Ms Haines highlighted that data collected by Audit+ will enable comparison between GP practices and help identify and share best practice. It was noted that the resource and audit would also support the new NSAID national prescribing indicator for 2017-2018 which is linked to CKD patients.

The Chairman opened discussion. The Chairman welcomed the opportunity to work with NWIS in the collection of real-time information and commented that the audit is easy to read and concise. Dr Black expressed his concerns in relation to the audit and his personal view that a high percentage of GPs would not use the audit. The Chairman welcomed Dr Rob Bracchi to the table who highlighted the advantages for GPs in using the audit. He confirmed that AWTTC would collate feedback from users. Clarification was sought in relation to the on-going work of CKD Assist initiative. The Chairman closed the discussion and confirmed AWMSG's support and general agreement that the audit would provide a good starter for the collection of clinically relevant and meaningful data.

Date of next meeting – Wednesday, 15th March 2017 in Abergavenny