

<b>Enclosure No:</b>	<b>1/AWMSG/1113</b>
<b>Agenda Item No:</b>	<b>5 – Minutes of previous meeting</b>
<b>Author:</b>	Chairman, AWMSG
<b>Contact:</b>	Tel: 029 20716900 E-Mail: awttc@wales.nhs.uk

## **ALL WALES MEDICINES STRATEGY GROUP (AWMSG)**

### **MINUTES OF THE AWMSG MEETING HELD ON WEDNESDAY, 16<sup>th</sup> OCTOBER 2013 COMMENCING 9.30 AM AT THE ANGEL HOTEL, ABERGAVENNY, NP7 5EN**

#### **VOTING MEMBERS PRESENT:**

**Did not  
participate in**

1.	Prof Philip Routledge	Chairman	
2.	Dr Fraser Campbell	GP with Prescribing Lead role	
3.	Prof David Cohen	Health Economist	
4.	Debbie Davies	Other professions eligible to prescribe	
5.	Mr Stuart Davies	Finance Director	<b>1-4</b>
6.	Dr Emma Mason	Clinical Pharmacologist	
7.	Mrs Susan Murphy	Managed Sector Primary Care Pharmacist	<b>12</b>
8.	Mr Stefan Fec	Community Pharmacist	
9.	Dr Stuart Linton	Hospital Consultant	
10.	Mr Christopher Palmer	Lay Member	
11.	Dr Klesh Sidhu	Welsh Health Specialised Services Committee	
12.	Mr Christian Smith	Senior Nurse	<b>7</b>
13.	Mr Lance Richard	ABPI Cymru Wales	
14.	Mr John Terry	Managed Sector Hospital Pharmacist	
15.	Prof John Watkins	Public Health Wales	<b>1-6</b>

#### **IN ATTENDANCE:**

16. Dr Robert Bracchi, NMG Chairman
17. Mrs Kath Haines, Head of WAPSU, AWTTTC
18. Mrs Ruth Lang, Head of Liaison & Administration, AWTTTC

#### **ALL WALES THERAPEUTICS & TOXICOLOGY CENTRE (AWTTC)**

##### **APPRAISAL LEADS:**

19. Mrs Gail Woodland, Senior Appraisal Pharmacist
20. Mrs Helen Adams, Senior Appraisal Pharmacist
21. Mrs Sabrina Rind, Senior Appraisal Pharmacist

AWMSG draft minutes  
Prepared by AWTTTC

## 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
CHMP	Committee for Medicinal Products for Human Use
DH	Department of Health
EMA	European Medicines Agency
FAR	Final Appraisal Recommendation
FDA	US Food and Drug Administration
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health Boards
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 Clinical Excellence
NMG	New Medicines Group
PAR	Preliminary Appraisal Recommendation
SMC	Scottish Medicines Consortium
TDAPG	Therapeutic Development Appraisal Partnership Group
T&FG	Task and Finish Group
WG	Welsh Government
WAPSU	Welsh Analytical Prescribing Support Unit
WPAS	Welsh Patient Access Scheme

### 1. Welcome and introduction

The Chairman welcomed AWMSG members. The Chairman confirmed that appraisal 1, elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (Stribild<sup>®</sup>▼) for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over who are antiretroviral-treatment-naïve or are infected with HIV-1 without known mutations associated with resistance to any of the three antiretroviral agents in Stribild, would be conducted in private as the submission is associated with a Wales Patient Access Scheme (WPAS) containing commercially sensitive information. He confirmed that the recommendation would be announced in public.

### 2. Apologies

Dr Karen Fitzgerald, Consultant in Pharmaceutical Public Health  
Dr Geoffrey Carroll, Welsh Health Specialised Services Committee  
Mr Roger Williams, Managed Sector Hospital Pharmacist  
Mr Rob Thomas, ABPI Cymru Wales  
Professor Roger Walker, Chief Pharmaceutical Officer

### Not in attendance

Dr Brendan Lloyd, Medical Director representative

### 3. Declarations of interest

Mr Christian Smith declared a personal specific interest in relation to Pfizer Ltd and the Chairman confirmed he would not participate or vote in the appraisal of pegvisomant (Somavert<sup>®</sup>). Mrs Susan Murphy declared a personal family interest in relation to GlaxoSmithKline Ltd and the Chairman confirmed she would not participate or vote in the reappraisal of pazopanib (Votrient<sup>®</sup>)

#### 4. Minutes of previous meeting

The minutes of the previous meeting were checked for accuracy. No changes were made.

Mr Stuart Davies joined the meeting.

#### 5. Appraisal 1 – Full submission (WPAS) – proceedings were conducted in private Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (Stribild<sup>®</sup>▼) for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over who are antiretroviral-treatment-naive or are infected with HIV-1 without known mutations associated with resistance to any of the three antiretroviral agents in Stribild

The Chairman welcomed representatives from the applicant company, Gilead Sciences Ltd.

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. There were none.

The Chairman announced the statement, pertinent to all appraisals, 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 Mrs Gail Woodland, AWTTTC assessment lead, to set the context of the appraisal. Mrs Woodland presented an overview of the submission as detailed in the ASAR and relayed the views of the clinical experts. Members were informed that a patient organisation submission had been received from the Terence Higgins Trust.

The Chairman invited Dr Bracchi, NMG Chairman, to provide a brief overview of the relevant issues identified in the preliminary appraisal. Dr Bracchi briefly summarised the issues discussed at NMG and relayed the preliminary recommendation that elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (Stribild<sup>®</sup>▼) should be recommended as an option for use within NHS Wales for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over who are antiretroviral-treatment-naive or are infected with HIV-1 without known mutations associated with resistance to any of the three antiretroviral agents in Stribild<sup>®</sup>▼. It was noted that this recommendation would apply only in circumstances where the approved Wales Patient Access Scheme is utilised.

The Chairman invited comment in relation to the case for clinical effectiveness. Clarification was sought in relation to renal impairment, monitoring and adherence. There was discussion over compliance. The Chairman referred members to the summary of clinical expert views. One of the clinical experts had identified a small proportion of patients with a low genetic barrier to resistance intolerant of, or ineligible for, Atripla<sup>®</sup>, who would benefit from a single once daily tablet regimen. Another expert considered that Stribild<sup>®</sup> may be used in patients in whom Eviplera<sup>®</sup> was not appropriate.

The Chairman invited Professor Cohen to comment on the case for cost effectiveness. Professor Cohen explained his role as AWMSG Health Economist and confirmed he had no input into the development of the ASAR, or discussions at NMG. Professor Cohen highlighted his observations from the ASAR and commented that the case for cost effectiveness had been well made by the applicant company.

The Chairman invited Mr Palmer to highlight salient issues within the patient organisation submission from the Terence Higgins Trust. Mr Palmer confirmed that the patient organisation welcomed the addition of a new treatment as it offered further treatment options for some

patients, including those who may be unable to tolerate other treatments. There were no other broader societal issues of note.

The Chairman referred to the applicant company response to the preliminary recommendation and offered opportunity to the delegates to highlight salient issues. Prior to concluding the discussion, the Chairman sought confirmation from the company delegates that the process had been fair and transparent. He thanked Gilead Sciences Ltd for engaging in the appraisal process, concluded appraisal proceedings and opened the meeting to the public.

**Appraisal decision subsequently announced:**

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

**Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (Stribild<sup>®</sup>▼) is recommended as an option for use within NHS Wales for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over who are antiretroviral-treatment-naïve or are infected with HIV-1 without known mutations associated with resistance to any of the three antiretroviral agents in Stribild<sup>®</sup>▼. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.**

**6. Chairman's report**

The Chairman confirmed that consultant on AWMSG's Strategy for 2013 to 2018 had commenced at the beginning of October. The Chairman asked members to consult with colleagues and submit comments to AWTTTC by the deadline of Thursday, 31<sup>st</sup> October 2013.

The Chairman confirmed that comments were being sought in relation to educational resource materials for the review of tramadol prescribing in NHS Wales which have been developed by AWTTTC on behalf of AWMSG. The Chairman encouraged members to submit comment on the educational pack at the earliest convenience.

The Chairman confirmed that Dr Phil Webb will be stepping down a deputy for Dr Geoffrey Carroll on AWMSG and will be replaced by Dr Khesh Sidhu. Dr Webb will represent Welsh Health Specialised Services Committee on the New Medicines Group and the Constitution of that Group is in the process of being updated to reflect this change in membership.

The Chairman confirmed Welsh Government's ratification of the advice announced at the May AWMSG meeting. The Chairman reminded members that ivacaftor (Kalydeco<sup>®</sup>) was not recommended for the treatment of cystic fibrosis in patients aged six years and older who have a G551D mutation in the CFTR gene. Members were informed that subsequent to the meeting, Welsh Government had issued a written statement confirming that the medicine would be made available in Wales due to issues relating to equity.

**Aclidinium bromide (Eklira<sup>®</sup> Genuair<sup>®</sup>▼) is recommended** as an option for use within NHS Wales as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease.

**Ferumoxytol (Rienso<sup>®</sup>▼) is recommended** as an option for restricted use within NHS Wales. Ferumoxytol (Rienso<sup>®</sup>▼) should only be used for the intravenous treatment of iron deficiency anaemia in non-haemodialysis dependent adult chronic kidney disease patients when oral iron is ineffective or cannot be used. Ferumoxytol (Rienso<sup>®</sup>▼) is not recommended for use within NHS Wales outside of this subpopulation of patients. The diagnosis of iron deficiency must be based on appropriate laboratory tests.

**Ingenol mebutate (Picato<sup>®</sup>) is recommended** as an option for use within NHS Wales for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis (AK) in adults.

**Linagliptin/metformin (Jentadueto<sup>®</sup>) is recommended** as an option for use within NHS Wales for the treatment of adult patients with type 2 diabetes mellitus:

- as an adjunct to diet and exercise to improve glycaemic control in adult patients inadequately controlled on their maximal tolerated dose of metformin alone, or those already being treated with the combination of linagliptin and metformin; and
- in combination with a sulphonylurea (i.e. triple combination therapy) as an adjunct to diet and exercise in adult patients inadequately controlled on their maximal tolerated dose of metformin and a sulphonylurea.

**Darunavir (Prezista<sup>®</sup>) 100 mg/ml oral suspension, co-administered with low dose ritonavir, is recommended** as an option for use within NHS Wales, in combination with other antiretroviral medicinal products, for the treatment of human immunodeficiency virus (HIV-1) infection in adult patients, as well as antiretroviral therapy-experienced paediatric patients from the age of 3 years and at least 15 kg body weight.

**Perampanel (Fycompa<sup>®</sup>) is recommended** as an option for restricted use within NHS Wales. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.

**Perampanel (Fycompa<sup>®</sup>) should be restricted** to treatment of patients whose seizures are still uncontrolled with first adjunctive therapy, within its licensed indication as adjunctive treatment of partial-onset seizures with or without secondarily generalised seizures in patients with epilepsy aged 12 years and older.

**Perampanel (Fycompa<sup>®</sup>) is not recommended** for use within NHS Wales outside of this subpopulation.

**Deferasirox (Exjade<sup>®</sup>) cannot be endorsed** for the treatment of chronic iron overload requiring chelation therapy when deferoxamine therapy is contraindicated or inadequate in patients with non-transfusion-dependent thalassaemia syndromes aged 10 years and older

**Levonorgestrel (Levosert<sup>®</sup>) cannot be endorsed** for the treatment of heavy menstrual bleeding

**Amlodipine besilate (Istin<sup>®</sup>) orodispersible tablets cannot be endorsed** for the treatment of hypertension, chronic stable angina pectoris and vasospastic (Prinzmetal's) angina

**Insulin degludec (Tresiba<sup>®</sup>) cannot be endorsed** for the treatment of diabetes mellitus in adults ( $\geq 18$  years)

**Insulin degludec/insulin aspart (Ryzodeg<sup>®</sup>) cannot be endorsed** for the treatment of diabetes mellitus in adults

**Colestilan (Bindren<sup>®</sup>) cannot be endorsed** for the treatment of hyperphosphataemia in adult patients with chronic kidney disease stage 5 receiving haemodialysis or peritoneal dialysis

Members were informed that on 2nd August 2013 a further notice of ratification was issued relating to the AWMSG advice announced at the June meeting:

**Ceftaroline fosamil (Zinforo<sup>®</sup>▼) is recommended as an option for restricted use within NHS Wales. Ceftaroline fosamil (Zinforo<sup>®</sup>▼) should be restricted to use** for the treatment of complicated skin and soft tissue infections in patients where methicillin-resistant *S. aureus* (MRSA) is suspected, only in the following settings:

- For infections caused by Gram-positive pathogens, only if intravenous (IV) vancomycin or IV teicoplanin is inappropriate, has not been tolerated or treatment modification is required; and IV daptomycin or IV linezolid is normally used.
- For mixed infections caused by common Gram-positive and Gram-negative pathogens (excluding extended-spectrum beta-lactamase-producing organisms, AmpC-producing organisms and non-fermenter Gram-negative organisms, such as *Pseudomonas aeruginosa*), only if IV vancomycin in combination with IV co-amoxiclav or IV teicoplanin in combination with IV co-amoxiclav is inappropriate, has not been tolerated or treatment modification is required; and IV daptomycin in combination with IV co-amoxiclav or IV linezolid in combination with IV co-amoxiclav is normally used.

**Ceftaroline fosamil (Zinforo<sup>®</sup>▼) is not recommended** for use within NHS Wales for the treatment of complicated skin and soft tissue infections outside of these settings.

**Ceftaroline fosamil (Zinforo<sup>®</sup>▼) is not recommended** for use within NHS Wales for the treatment of community-acquired pneumonia.

**Adalimumab (Humira<sup>®</sup>) is recommended** for use within NHS Wales for the treatment of adults with severe axial spondyloarthritis without radiographic evidence of ankylosing spondylitis but with objective signs of inflammation by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI), who have had an inadequate response to, or are intolerant to non steroidal anti-inflammatory drugs (NSAIDs).

**C1-esterase inhibitor (Berinert<sup>®</sup>) is recommended as an option** for use within NHS Wales for the treatment of acute episodes of hereditary angioedema type I and II. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.

**Cefuroxime (Aprokam<sup>®</sup>) cannot be endorsed** for antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery. Consideration should be given to official guidance on the appropriate use of antibacterial agents, including guidance on the antibiotic prophylaxis on eye surgery.

**Ethinylestradiol/drospirenone (Flexyess<sup>®</sup>) cannot be endorsed** as oral contraception.

**Canakinumab (Ilaris<sup>®</sup>) cannot be endorsed** for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) in children aged 2 to < 4 years.

**Aciclovir lauriad (Sitavig<sup>®</sup>) cannot be endorsed** for the treatment of recurrent herpes labialis in immunocompetent adults with frequent herpes episodes.

The Chairman confirmed that on 16<sup>th</sup> August the Service had been informed of Welsh Government's ratification of the following AWMSG advice announced at the July meeting:

**Lapatinib (Tyverb<sup>®</sup>) is recommended as an option for restricted use** within NHS Wales for the treatment of adult patients with breast cancer, whose tumours overexpress HER2 (ErbB2), in combination with capecitabine for patients with advanced or metastatic disease with progression following prior therapy, which must have included anthracyclines and taxanes and therapy with trastuzumab in the metastatic setting. Lapatinib (Tyverb<sup>®</sup>) should be restricted within its licensed indication for the treatment of patients as an alternative to treatment with trastuzumab and capecitabine or trastuzumab and vinorelbine in patients in whom clinicians consider this clinically appropriate. Lapatinib (Tyverb<sup>®</sup>) 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 is utilised.

**Nepafenac (Nevanac®) is recommended for use** within NHS Wales for reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients.

**Ulipristal acetate (Esmya®) is recommended as an option for use** within NHS Wales for the pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The duration of treatment is limited to three months.

**Adalimumab (Humira®) is recommended as an option for use** within NHS Wales for the treatment of severe active Crohn's disease in paediatric patients (6 to 17 years of age) who have had an inadequate response to conventional therapy including primary nutrition therapy, a corticosteroid, and an immunomodulator, or who are intolerant to or have contraindications for such therapies.

**Adalimumab (Humira®) is recommended as an option for use** within NHS Wales, in combination with methotrexate, for the treatment of active polyarticular juvenile idiopathic arthritis, in children aged 2 to 4 years who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs). Adalimumab can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate. Adalimumab has not been studied in children aged less than 2 years.

**Tenofovir disoproxil (as fumarate) (Viread®) film-coated tablets are recommended as an option for use** within NHS Wales in combination with other antiretroviral medicinal products for the treatment of HIV-1-infected adolescent and paediatric patients, with nucleoside reverse transcriptase inhibitor (NRTI) resistance or toxicities precluding the use of first line agents, aged 12 to < 18 years (245 mg tablets) and aged 6 to < 12 years who weigh from 17 kg to less than 22 kg (123 mg tablets), 22 kg to less than 28 kg (163 mg tablets) and 28 kg to less than 35 kg (204 mg tablets) and **33 mg/g granules are recommended as an option for use** within NHS Wales in combination with other antiretroviral medicinal products for the treatment of HIV-1 infected paediatric patients, with NRTI resistance or toxicities precluding the use of first line agents, from 2 to < 6 years of age, and above 6 years of age for whom a solid dosage form is not appropriate. The choice of tenofovir disoproxil to treat antiretroviral-experienced patients with HIV-1 infection should be based on individual viral resistance testing and/or treatment history of patients.

**Tenofovir disoproxil (as fumarate) (Viread®) 245 mg film-coated tablets are recommended for use** within NHS Wales for the treatment of chronic hepatitis B in adolescents 12 to < 18 years of age with compensated liver disease and evidence of immune active disease, i.e. active viral replication, persistently elevated serum ALT levels and histological evidence of active inflammation and/or fibrosis and **33 mg/g granules are recommended for use** within NHS Wales for the treatment of chronic hepatitis B in adolescents 12 to < 18 years of age for whom a solid dosage form is not appropriate with: compensated liver disease and evidence of immune active disease, i.e. active viral replication, persistently elevated serum ALT levels and histological evidence of active inflammation and/or fibrosis.

In the absence of a submission from the holder of the marketing authorisation, the following Statements of Advice had been ratified by Welsh Government. The Chairman reiterated the following medicines should not be funded routinely within NHS Wales:

**iron (III) isomaltoside 1000 (Diafer®) cannot be endorsed** for the treatment of iron deficiency in adult patients with chronic kidney disease on dialysis.

**c1-esterase inhibitor (Berinert®) cannot be endorsed** for the pre-procedure prevention of acute episodes of hereditary angioedema type I and II (HAE).

The Chairman reported that an AWMSG training day for members of AWMSG and NMG had been held on 4<sup>th</sup> September. He thanked Professor David Cohen and Professor Dyfrig Hughes for their input on the day.

Members were informed that AWMSG's Patient and Public Interest Group held its inaugural meeting on Wednesday, 9<sup>th</sup> October 2013 in the Academic Centre Llandough. There was discussion over the strategic priorities for patient engagement, a talk on 'Patients' medicine taking behaviour', and the lay members of AWMSG and NMG shared their experiences with representatives of patient organisations. The Chairman confirmed that AWTTTC is developing a strategy for patient engagement which will be presented to AWMSG early next year.

The Chairman announced an AWMSG Masterclass will be held for members of ABPI Cymru Wales and the Ethical Medicines Industry Group on Tuesday, 26<sup>th</sup> November at the All Nations Centre when representatives of AWTTTC will update industry colleagues on the HTA process in Wales and other aspects of the work of AWMSG.

The Chairman announced the appraisals scheduled for the next AWMSG meeting to be held in Cardiff on Wednesday, 20<sup>th</sup> November 2013 commencing 9.30 am. It was highlighted that all meeting documentation would be available on the AWMSG website prior to the meeting.

**Appraisal 1: Full Submission**

**Botulinum toxin type A (Botox®)** for the management of urinary incontinence in adult patients with neurogenic detrusor overactivity due to subcervical spinal cord injury (traumatic or non-traumatic) or multiple sclerosis, who are not adequately managed with anticholinergics; patients should be already catheterising or willing and able to catheterise if required

**Applicant Company: Allergan Ltd**

**Appraisal 2: Limited Submission**

**Etravirine (Intelence®)** in combination with a boosted protease inhibitor and other antiretroviral medicinal products, for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-experienced paediatric patients from 6 years to less than 18 years of age

**Applicant Company: Janssen-Cilag Ltd**

**Appraisal 3: Limited Submission**

**Saxagliptin (Onglyza®)** in adult patients aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control as triple oral therapy in combination with metformin plus a sulphonylurea when this regimen alone, with diet and exercise, does not provide adequate glycaemic control

**Applicant Company: Bristol-Myers Squibb Pharmaceuticals Ltd/AstraZeneca UK Ltd**

**Appraisal 4: Limited Submission**

**Sodium phenylbutyrate (Pheburane®)** for adjunctive therapy in the chronic management of urea cycle disorders, involving deficiencies of carbamylphosphate synthetase, ornithine transcarbamylase or argininosuccinate synthetase. It is indicated in all patients with neonatal-onset presentation (complete enzyme deficiencies, presenting within the first 28 days of life) and in patients with late-onset disease (partial enzyme deficiencies, presenting after the first month of life) who have a history of hyperammonaemic encephalopathy

**Applicant Company: Lucane Pharma**

**Appraisal 5: Full Submission**

**Lixisenatide (Lyxumia®)** for the treatment of adults with type 2 diabetes mellitus to achieve glycaemic control in combination with oral glucose-lowering medicinal products and/or basal insulin when these, together with diet and exercise, do not provide adequate glycaemic control

**Applicant Company: Sanofi-Aventis Ltd**



### **Appraisal 6: Limited Submission**

**Etanercept (Enbrel®)** for the treatment of polyarthritis (rheumatoid factor positive or negative) from 2-4 years of age and extended oligoarthritis in children and adolescents from the age of 2 years who have had an inadequate response to, or who have proved intolerant of, methotrexate. Treatment of psoriatic arthritis in adolescents from the age of 12 years who have had an inadequate response to, or who have proved intolerant of, methotrexate. Treatment of enthesitis-related arthritis in adolescents from the age of 12 years who have had an inadequate response to, or who have proved intolerant of, conventional therapy

**Applicant Company: Pfizer Ltd**

The Chairman reminded members to declare any interests pertinent to the appraisals scheduled. The Chairman invited patients, patient organisations and patient carers to submit their views in relation to medicines scheduled for appraisal, and suggested they contact Ruth Lang at AWTTTC for further information in relation to the future work programme.

**7. Appraisal 2 – Full submission (reappraisal at the direction of Welsh Government)**  
**Pegvisomant (Somavert®) is indicated for the treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise IGF-I concentrations or was not tolerated**

The Chairman confirmed that Pfizer had declined the invitation to input into the appraisal.

Mr Christian Smith left the meeting. The Chairman invited remaining members to declare any interests in either the applicant company or the medicine if they had not already done so. There were no further declarations.

The Chairman announced the statement, pertinent to all appraisals, 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 Mrs Gail Woodland, AWTTTC assessment lead, to set the context of the appraisal. Mrs Woodland presented an overview of the submission as detailed in the ASAR. Mrs Woodland explained that in line with the NICE accreditation process, AWTTTC had reviewed negative AWMSG recommendations and had invited applicant companies to re-engage in the appraisal process. Although Pfizer had declined this opportunity, Welsh Government had instructed AWMSG to re-appraise using information previously submitted by Pfizer Ltd and any new information available in the public domain. Mrs Woodland relayed the views of the clinical experts and confirmed the number of patients considered by the clinicians to be eligible for treatment within Wales was significantly lower than the numbers suggested by the company. One expert suggested a maximum of one new patient per year. Another expert would like to prescribe pegvisomant for three of their current patients. The experts agreed that there were a small minority of patients in whom currently available treatment options fail to achieve adequate biochemical control and who have active, symptomatic acromegaly, with reduced quality of life as a result. It was suggested that these patients could potentially benefit from treatment with a growth hormone receptor antagonist. One expert stated that pegvisomant is used widely outside of Wales in the treatment of patients with acromegaly. Members were informed that a patient organisation submission had been received from the Pituitary Foundation. Mrs Woodland highlighted that this had been received after the NMG meeting and had therefore not been considered by NMG when making their recommendation to AWMSG.

Dr Bracchi provided an overview of the issues highlighted at NMG and relayed their view that pegvisomant (Somavert®) should not be recommended for use within NHS Wales for the treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise IGF-I concentrations or was not tolerated. It was reported that NMG had considered the case for clinical effectiveness had been made, but the case for cost effectiveness had not. NMG did not consider that pegvisomant (Somavert®) met the AWMSG criteria for ultra orphan medicine status.

The Chairman opened the discussion and there were no outstanding issues relating to clinical effectiveness. Members considered the summary of evidence on budget impact within the ASAR. Clarification was sought in relation to the number of clinical experts who had provided views. It was noted that one expert had declared a personal specific interest in relation to pegvisomant for the indication under consideration.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. It was noted that this medicine had previously been designated an orphan medicine, but had been withdrawn from the European Medicines Agency register of orphan medicines in November 2012 at the end of the period of market exclusivity. Professor Cohen summarised his observations in relation to the health economics and confirmed that the incremental cost-effectiveness ratio far exceeded the threshold cost-effectiveness range. Members sought clarification of the number of patients who may be eligible for treatment and referred to the clinical expert summary. It was noted that one expert had stated that 5–7 new acromegaly patients undergo surgery each year within their catchment area, which covers the South and Mid Wales population (approximately 2.5 million people). Of these 50%–60% would be expected by the expert to be cured by surgery, with a further 30%–40% entering remission in response to treatment with somatostatin analogues and/or radiotherapy. The expert suggested a maximum of 10% of new patients per year in Wales (approximately 0–1) would be eligible to receive treatment with pegvisomant (Somavert®). The expert envisaged using pegvisomant only in patients who have failed to achieve adequate biochemical control with all other treatment modalities. Another expert identified three eligible patients. It was noted that one expert suggested that pegvisomant is used widely outside of Wales in the treatment of patients with acromegaly.

The Chairman reminded members of their responsibility to consider broader societal issues. Mr Palmer presented a comprehensive patient organisation submission from The Pituitary Foundation. Mr Palmer drew members' attention to the case studies and highlighted that this medicine is the last option for patients with uncontrollable acromegaly. He relayed the view that for the small selected few who need this medicine it is hugely beneficial. They are patients who are very unwell and giving them an opportunity to access this medicine could vastly improve their quality of life and reduce risks of co-morbidities and improve longer term prognosis.

Having confirmed that there were no outstanding issues the Chairman concluded the appraisal.

**Appraisal decision subsequently announced:**

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

**Pegvisomant (Somavert®) is not recommended for use within NHS Wales for the treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise IGF-I concentrations or was not tolerated. The case for cost effectiveness has not been proven.**

## 8. Appraisal 3 – Full submission

### **Tegafur/gimeracil/oteracil (Teysuno<sup>®</sup>▼) for the treatment of advanced gastric cancer in adults when given in combination with cisplatin**

The Chairman welcomed representatives from the applicant company, Nordic Pharma Ltd. Mr Christian Smith rejoined the meeting. The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. There were none.

The Chairman alluded to the statement, pertinent to all appraisals, 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 Mrs Helen Adams, AWTTTC assessment lead, to set the context of the appraisal. Mrs Adams presented an overview of the submission as detailed in the ASAR and relayed the views of the clinical experts. Members were informed that a patient organisation submission had not been received.

The Chairman invited Dr Bracchi, NMG Chairman, to provide a brief overview of the relevant issues identified in the preliminary appraisal. Dr Bracchi briefly summarised the issues discussed at NMG and relayed the preliminary recommendation of NMG that tegafur/gimeracil/oteracil (Teysuno<sup>®</sup>▼) should be recommended as an option for restricted use within NHS Wales in adults for the treatment of advanced gastric cancer when given in combination with cisplatin, when standard triplet therapy is not suitable.

The Chairman opened discussion and members considered the case for clinical effectiveness. Members considered the trial data and asked how responses were measured. There was discussion in relation to the indirect comparison and patient populations. The company representatives provided the rationale for using different doses in the study. The Chairman referred members to clinical expert summary. It was noted that doublet regimes are not generally used often within their practice, but would be used occasionally in patients where there is concern about cardiac function. These doublet regimen was suggested to be oral capecitabine (625 mg/m<sup>2</sup> twice daily on days 1–21 days of a three-week cycle) plus oxaliplatin (130 mg/m<sup>2</sup> as continuous intravenous infusion on day 1); very occasionally a regimen comprising paclitaxel (175 mg/m<sup>2</sup>) plus carboplatin (dose determined by area under the curve and glomerular filtration rate) would be used if there was concern regarding cardiac function or marked capecitabine toxicity. However, the expert suggested that if there is concern about the patient not being fit enough to tolerate treatment then often the decision not to treat is the correct one. The expert was unsure about practice elsewhere in Wales, but suggested that it would be similar. It was noted that capecitabine is now well established as a treatment for several malignancies, but does have drawbacks with regard to side-effects, especially cardiotoxicity and hand foot syndrome. It was suggested that Teysuno<sup>®</sup>▼ seems to be less toxic but as effective as capecitabine, based on research papers read by one expert.

Professor Cohen commented on the case for cost-effectiveness and highlighted the salient aspects from the ASAR. Professor Cohen explained the differences between financial costs and the economic case. The company delegates justified their approach in providing a cost minimisation analysis in that they considered it the most pragmatic approach for presenting the analysis. Members took account of the summary on budget impact. It was confirmed that a patient organisation submission had not been received. Mr Palmer informed members of the organisations that had been approached by AWTTTC. The company representatives confirmed there is no homecare provision for this medicine. There were no other societal issues of note.

The Chairman referred to the applicant company response to the preliminary recommendation and offered opportunity to the delegates to highlight salient issues. Prior to concluding the discussion, the Chairman sought confirmation from the company delegates that the process had been fair and transparent. He thanked Nordic Pharma Ltd for engaging in the appraisal process and proceeded to the next appraisal.

**Appraisal decision subsequently announced:**

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:

**Tegafur/gimeracil/oteracil (Teysuno<sup>®</sup>▼) is recommended as an option for restricted use within NHS Wales in adults for the treatment of advanced gastric cancer when given in combination with cisplatin, when standard triplet therapy is not suitable.**

**9. Appraisal 4 – Full submission  
5-aminolaevulinic acid (Ameluz<sup>®</sup>▼) for the treatment of actinic keratosis of mild to moderate intensity on the face and scalp (Olsen grade 1 to 2)**

The Chairman welcomed representatives from the applicant company, Spirit Healthcare Ltd.

There were no declarations of interests in either the applicant company or the medicine and the Chairman commenced the appraisal proceedings.

The Chairman announced the statement, pertinent to all appraisals, 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 Mrs Sabrina Rind, AWTTTC assessment lead, to set the context of the appraisal. Mrs Rind presented an overview of the submission as detailed in the ASAR. Dr Bracchi, NMG Chairman, provided an overview of the relevant issues identified in the preliminary appraisal. Dr Bracchi briefly summarised the issues discussed and relayed the view of NMG that 5-aminolaevulinic acid (Ameluz<sup>®</sup>▼) should be recommended as an option for restricted use within NHS Wales for the treatment of actinic keratosis of mild to moderate intensity on the face and scalp (Olsen grade 1 to 2) when photodynamic therapy (PDT) is considered appropriate. Dr Bracchi confirmed NMG were of the view that the company submission provided evidence of the clinical and cost effectiveness of 5-aminolaevulinic acid (Ameluz<sup>®</sup>▼) compared to methylaminolevulinate (Metvix<sup>®</sup>) and should therefore be used when PDT is considered appropriate.

The Chairman invited members to consider the case for clinical effectiveness and highlight any outstanding issues. Clarification was sought in relation to re-treatment. The company delegates confirmed that no data was collected on quality of life. The company delegates provided the rationale for switching their non-inferiority approach in line with EMA regulations and asked that this be included in the ASAR. The Chairman confirmed that additional information could not be accepted at this stage in the process. The Chairman referred members to the summary of clinical expert views. The clinical experts stated that actinic keratoses do not necessarily require treatment especially if the patient is not troubled by the lesions. The experts outlined the current treatment options available in Wales:

One clinical expert highlighted the benefits of PDT. It was stated that PDT is useful in the treatment of patients with sun damaged skin as it treats field change. They added that PDT is less time consuming for the patient and is associated with good results and cosmetic outcome.

It was noted that PDT does not work well on thickened areas of skin. No unmet clinical need was highlighted.

The Chairman invited Professor Cohen to comment on the case for cost effectiveness. Professor Cohen highlighted the limitations in the submission presented by the company. It was confirmed that no patient organisation submission had been received. There were no outstanding societal or budget impact issues of note.

The Chairman referred to the applicant company response to the preliminary recommendation and offered opportunity to the delegates to highlight salient issues. Prior to concluding the discussion, the Chairman sought confirmation from the company delegates that the process had been fair and transparent. He thanked Spirit Healthcare for engaging in the appraisal process and proceeded to the next appraisal.

**Appraisal decision subsequently announced:**

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:

**5-aminolaevulinic acid (Ameluz<sup>®▼</sup>) is recommended as an option for restricted use within NHS Wales for the treatment of actinic keratosis of mild to moderate intensity on the face and scalp (Olsen grade 1 to 2) when photodynamic therapy is considered appropriate.**

**10. Appraisal 5 – Full submission**

**Lisdexamfetamine dimesylate (Elvanse<sup>®▼</sup>) as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children aged 6 years of age and over when response to previous methylphenidate treatment is considered clinically inadequate. Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural disorders**

The Chairman welcomed the representative from the applicant company, Shire Pharmaceuticals Ltd

The Chairman reminded members to declare any interests in either the applicant company or the medicine if they had not already done so. There were none.

The Chairman alluded to the statement, pertinent to all appraisals, 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 Mrs Helen Adams, AWTTTC assessment lead, to set the context of the appraisal. Mrs Adams presented an overview of the submission as detailed in the ASAR. She confirmed that a patient organisation submission had been received from the Attention Deficit Disorder Information and Support Service.

The Chairman invited Dr Bracchi, NMG Chairman, to provide an overview of the relevant issues identified in the preliminary appraisal. Dr Bracchi briefly summarised the issues discussed at NMG and confirmed that NMG had supported the use of lisdexamfetamine dimesylate (Elvanse<sup>®▼</sup>) for use within NHS Wales as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children aged six years of age and over when response to previous methylphenidate treatment is considered clinically inadequate. Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural disorders.

The Chairman invited comment in relation to the case for clinical effectiveness. Clarification was sought in relation to the rating scales as members tried to put the evidence provided into context. Members explored rates of retention and withdrawal, adverse events and monitoring requirements. The company delegates were asked to explain what the 'comprehensive treatment programme' entailed. Members also considered that the marketing authorisation allows patients to continue therapy into adulthood.

The Chairman referred members to the summary of clinical expert views. The clinical experts identified methylphenidate and atomoxetine as the current treatment options, with the former being more prevalent in the cohort under consideration. It was noted that methylphenidate was their preferred treatment. The clinical experts suggested that lisdexamfetamine dimesylate could be used when maximum doses of methylphenidate and atomoxetine were ineffective or in the event of adverse reactions to either of these treatments. Experts commented that lisdexamfetamine dimesylate has potential value for a few patients, as it is the only ADHD preparation that can be dissolved in water, providing an option where capsules could not be tolerated. Apart from that, methylphenidate treatment is usually limited by side effects rather than lack of effect and lisdexamfetamine dimesylate has effectively the same side effect profile, so they did not consider that there would be many occasions when someone would switch from methylphenidate to lisdexamfetamine dimesylate. It was suggested that use would be limited to a very small number of patients.

The Chairman moved on to the case for cost effectiveness and asked Professor Cohen to comment on the evidence. There were no outstanding issues and the Chairman referred members to the summary of budget impact.

Mr Palmer confirmed that the Attention Deficit Disorder Information and Support Service welcomed this medicine as an alternative treatment option. He read an extract from the patient organisation submission highlighting the benefits of this treatment. The wider societal issues were noted.

The Chairman referred to the applicant company response to the preliminary recommendation and offered opportunity to the delegates to highlight salient issues. Prior to concluding the discussion, the Chairman sought confirmation from the company delegates that the process had been fair and transparent. He thanked Shire Pharmaceuticals Ltd for engaging in the appraisal process and proceeded to the next appraisal.

#### **Appraisal decision subsequently announced:**

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:

**Lisdexamfetamine dimesylate (Elvanse<sup>®</sup>▼) is recommended as an option for use within NHS Wales as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children aged six years of age and over when response to previous methylphenidate treatment is considered clinically inadequate. Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural disorders.**

#### **11. Appraisal 6 – Limited submission Raltegravir (Isentress<sup>®</sup>) in combination with other anti-retroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection in adolescents and children from the age of 2 years**

The Chairman welcomed representation from the applicant company, Merck Sharp and Dohme Ltd.

The Chairman reminded members to declare any interests in either the applicant company or the medicine if they had not already done so. There were none.

The Chairman alluded to the statement, pertinent to all appraisals, 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 Mrs Sabrina Rind, AWTTTC assessment lead, to set the context of the appraisal. Mrs Rind explained that this application had met AWMSG's criteria for a limited submission. Mrs Rind highlighted that the applicant company had submitted evidence for a sub-population, for use in paediatric patients who are resistant or intolerant to non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (PIs), or for whom these options are compromised due to drug-drug interactions. Mrs Rind presented an overview of the ASAR and confirmed that no clinical expert or patient views had been received.

Dr Bracchi briefly summarised the issues discussed at NMG and confirmed that NMG supported use of this medicine within NHS Wales for the indication being appraised (i.e. the sub-population). There were no societal or budget impact issues of note.

The Chairman referred to the applicant company response to the preliminary recommendation and offered opportunity to the delegates to highlight salient issues. Prior to concluding the discussion, the Chairman sought confirmation from the company delegates that the process had been fair and transparent. He thanked Merck Sharp and Dohme Ltd for engaging in the appraisal process and proceeded to the next appraisal.

**Appraisal decision subsequently announced:**

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:

**Raltegravir (Isentress<sup>®</sup>) 25 mg and 100 mg chewable tablets, in combination with other anti-retroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection in children aged 2–11 years are recommended as an option for restricted use within NHS Wales.**

**Raltegravir (Isentress<sup>®</sup>) 400 mg film-coated tablets, in combination with other anti-retroviral medicinal products for the treatment of HIV-1 infection in adolescents and children from the age of 6 years and weighing  $\geq$  25 kg, are recommended as an option for restricted use within NHS Wales.**

**Raltegravir (Isentress<sup>®</sup>) 25 mg and 100 mg chewable tablets and 400 mg film-coated tablets should be restricted for use in patients who are resistant or intolerant to non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (PIs), or for whom these options are compromised due to drug–drug interactions.**

**12. Reappraisal following Independent Review**

**Pazopanib (Votrient<sup>®</sup>) for the treatment of adult patients with selective subtypes of advanced soft tissue sarcoma who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy**

Mrs Susan Murphy left the meeting. No further declarations of interest were noted.

The Chairman welcomed delegates representing GlaxoSmithKline.

The Chairman confirmed that Professor John Watkins, Mr John Terry and Professor David Cohen would participate in the discussion but would not vote, as they had been part of the independent review which had determined whether the grounds for appeal, as set out by GlaxoSmithKline, had been met.

The Chairman alluded to the statement, pertinent to all appraisals, 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 Mrs Gail Woodland, AWTTTC assessment lead, to set the context of the appraisal. Mrs Woodland provided the background and explained that on 20<sup>th</sup> March 2013 AWMSG appraised pazopanib (Votrient<sup>®</sup>▼) and did not recommend its use within NHS Wales. In line with the AWMSG appraisal process, the applicant company, GlaxoSmithKline (GSK), had ten days to accept this recommendation or lodge a request for an independent review. AWTTTC received a request, dated 4<sup>th</sup> April 2013, outlining the company's concerns in relation to the interpretation of the evidence. An Independent Review was convened on Wednesday, 18<sup>th</sup> September 2013, to consider the issues raised by the company in response to the final appraisal recommendation. The Panel agreed that there may have been uncertainty or misinterpretation of the evidence, and recommended that AWMSG should reconsider the evidence submitted and Final Appraisal Recommendation.

Professor John Watkins, who Chaired the Independent Review (IR) Panel, provided an overview of the issues identified in the review:

- In line with the ASAR, the IR panel agreed that the company had made considerable efforts to estimate the cost-effectiveness of pazopanib (Votrient<sup>®</sup>▼) for the treatment of STS patients. However, the panel considered that the case for cost effectiveness had not been proven and could not be made.
- There are two treatment options currently available within NHS Wales which do not have the same level of evidence as pazopanib (Votrient<sup>®</sup>▼).
- Pazopanib (Votrient<sup>®</sup>▼) is the only product that has high quality Phase III trial data.
- There is no evidence that pazopanib (Votrient<sup>®</sup>▼) is less effective than other available treatments.
- Pazopanib (Votrient<sup>®</sup>▼) is cost saving compared to other treatment options, based on acquisition and administrative costs.
- The financial risk of pazopanib (Votrient<sup>®</sup>▼) is deemed to be 'low' based on the limited survival of patients and overall patient numbers.
- The panel agreed with AWMSG that pazopanib (Votrient<sup>®</sup>▼) does not meet the criteria for ultra orphan drug status; however, they recognised that this is a very rare disease.
- The panel considered that there were advantages to pazopanib (Votrient<sup>®</sup>▼) being an oral therapy in terms of patient choice, patient safety and patient acceptability when compared to therapies which require a central line. In addition, there are issues in relation to delivery of care with therapies that require central line insertion.



Professor Watkins confirmed the decision of the IR Panel: was that the grounds for review were upheld and the decision of the IR Panel was that AWMSG should reappraise pazopanib (Votrient<sup>®</sup>) taking account of the issues highlighted above.

The Chairman opened the discussion and invited comment in relation to the case for clinical effectiveness. Clarification was sought in relation to the improvements in quality of life and monitoring. The Chairman referred members to the summary of clinical expert views. It was noted that a number of treatment options are available for metastatic soft tissue sarcoma. The clinicians felt that, although it would not directly displace any of the treatments in the current pathway, pazopanib is an attractive option because it is an oral, non-toxic treatment. A suggestion was made that it would probably be used after second or third line chemotherapy, when the patient was less well and the chance of response with “conventional” chemotherapy is less.

Professor Cohen commented on the case for cost effectiveness. It was noted that a discount would be available to NHS Wales via a Department of Health approved Patient Access Scheme. Professor Cohen queried whether best supportive care was the most appropriate comparator based on clinical expert advice. Clarification was sought in relation to post progression survival in the economic model. The challenge in producing robust cost effectiveness evidence was acknowledged because of the rarity of the disease. As pazopanib is available via the Cancer Drugs Fund in England, member queries whether any data had been collected from patient outcomes in relation to quality of life. The company delegates confirmed that no patient outcome data had been collected. The Chairman referred members to the summary of evidence on budget impact.

Mr Palmer relayed the view of Sarcoma UK that sarcoma patients have a difficult pathway to treatment. The 5 year survival is approximately 55% but the figure for those with advanced disease is <10%. Many sarcoma patients are disabled by primary treatment with consequent multiple problems. Advanced metastatic sarcoma offers median 12 months survival. The current treatment is chemotherapy which requires regular hospital attendance for intravenous treatment of finite duration – usually 6 cycles per drug. Chemotherapy is highly toxic with unpleasant side effects, low response rate and almost certain disease progression. Despite this sarcoma patients can often retain a good quality of life until late in the progress of the disease pazopanib (Votrient<sup>®</sup>) offers longer progression-free intervals and survival benefits while retaining a high quality of life. There are fewer toxic side effects, although there are limitations which will make some patients ineligible and cause some patients to stop treatment. Pazopanib (Votrient<sup>®</sup>) is an oral, self-managed treatment, cutting down hospital visits and eliminating needles, and is taken for as long as the patient responds. Sarcoma UK acknowledged that no cancer therapy is without challenges for the patients, but the advent of an oral therapy with fewer side effects and longer survival is a true step forward.

The Chairman referred to the applicant company’s ground for appeal and offered opportunity to the delegates to highlight salient issues. A closing statement was read, and the delegates confirmed they were satisfied that all the outstanding issues had been adequately addressed. The Chairman sought confirmation from the company delegates that the process had been fair and transparent. He thanked GlaxoSmithKline for engaging in the appraisal process and closed proceedings.

**Appraisal decision subsequently announced:**

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:

**Pazopanib (Votrient<sup>®</sup>) is recommended as an option for use within NHS Wales for the treatment of adult patients with selective subtypes of advanced soft tissue sarcoma (STS) who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy. This recommendation applies only in circumstances where the approved Patient Access Scheme is utilised.**

**13. AWPAG update (draft minutes of July 2013 meeting)**

The draft minutes of the AWPAG meeting were presented to members for information. Concern was expressed over the potential risk to patients on biologics receiving a live vaccine. Dr Linton agreed to outline his concerns and submit to AWTTTC outside of the meeting.

**14. Primary Care Prescribing Analysis- Gluten Free**

Ms Kath Haines presented Enclosure 10/AWMSG/1013 and asked AWMSG to consider the prescribing analysis of gluten-free products following implementation of the AWMSG guidance, and note the cost difference between “off the shelf” and tariff prices of gluten-free products.

**15. Tramadol and Morphine**

**National Prescribing Indicator (NPI) report**

Ms Haines presented Enclosure 11/AWMSG/1013 and asked AWMSG to review the report outlining prescribing against selected National Prescribing Indicators (NPIs) and local comparators. Members were informed that in addition to the quarterly NPI reports, the Welsh Analytical Prescribing Support Unit intends to provide more detailed information on specific NPIs individualised to health board and locality cluster. Ms Haines explained the report provides prescribing information on the morphine NPI and also the tramadol local comparator. Morphine items as a percentage of strong opioid items has been included as an NPI since April 2012, to encourage morphine to be considered as the first-line strong opioid of choice where appropriate. The prescribing of tramadol has been monitored as a local comparator since April 2009. Tramadol is subject to abuse and dependence and 175 deaths related to the misuse of tramadol were reported in England and Wales in 2012. In light of this information and concerns raised by Welsh Government, the All Wales Prescribing Advisory Group has proposed that monitoring of tramadol prescribing be included as an NPI for 2014–2015.

**16. NPI Quarterly Report**

Ms Haines presented Enclosure 13/AWMSG/1013 and asked AWMSG to note the position of health boards within NHS Wales with respect to the National Prescribing Indicator (NPI) data to June 2013, which is the most recent quarterly prescribing information available. She explained the purpose of the paper is to report on the position of each health board against each NPI as at June 2013. The threshold for each prescribing indicator is set at the 25<sup>th</sup> percentile (i.e. reducing or increasing prescribing rates in line with the best performing 25% of practices). For the 2013–2014 NPIs, the prescribing data for all general practices in Wales for the quarter ending 31 December 2012 has been utilised. All practices within health boards are encouraged to achieve or move towards these thresholds.

**17. Prescribing of Denosumab (Prolia<sup>®</sup>) in Wales (Review)**

The Chairman invited Dr Tessa Lewis, AWTTTC Medical Adviser, to present Enclosure 13/AWMSG/1013. She explained that the AWMSG guidance document “Prescribing of Denosumab (Prolia<sup>®</sup>) in Wales” (2011) had been reviewed by a working group and a shared care protocol, led by Mr Alan Clatworthy, was being presented for endorsement by AWMSG. The guidance relates to the use of denosumab at a dose of 60 mg for the prevention of osteoporotic fractures in postmenopausal women, in accordance with the guidelines (NICE TA204). The Chairman asked members for comment. It was noted that the updated document included additional monitoring requirements. There was discussion over the availability of vitamin D testing and the organisational ability within general practices to set up shared care arrangements. There was also discussion in relation to the level of uptake of the AWMSG guidance and it was suggested that the wording ‘to ensure uptake’ should be amended to ‘improve the uptake’. The Chairman asked Dr Lewis to relay AWMSG’s comments back to the

working group and confirmed the general support of AWMSG.

**18. All Wales Risk/ Benefit Assessment Tool for Oral Anticoagulant Treatment in People with Atrial Fibrillation**

Dr Tessa Lewis presented Enclosure 12/AWMSG/1013 and asked AWMSG to comment on the All Wales Risk/Benefit Assessment Tool for Oral Anticoagulant Treatment in People with Atrial Fibrillation. She explained the purpose of the document - following the publication of the All Wales advice on the role of oral anticoagulants for the prevention of stroke and systemic embolism in people with atrial fibrillation, the need for an All Wales risk/benefit assessment for oral anticoagulant treatment in people with atrial fibrillation was raised. Dr Lewis acknowledged Mrs Louise Howard-Baker, AWPAG Chair, who had led on this work. The tool supports a consistent approach for people with atrial fibrillation, both in hospital and GP settings, to promote:

- an assessment of stroke risk,
- an assessment of bleeding risk,
- effective annual assessment, and
- data collection/audit trail.

It was noted the All Wales Prescribing Advisory Group (AWPAG) recommends that the necessary IT systems are put in place to promote the use of this tool. Dr Lewis highlighted that the work pertained to recommendation 19 of the AWMSG Medicines Strategy for Wales:

*“AWMSG will work with clinical networks and Specialist groups to ensure that national clinical pathways and guidance include consistent advice on cost effective and evidence-based prescribing.”*

The Chairman confirmed AWMSG's endorsement of the template and requested that the document be reviewed in light of the subsequent publication of any NICE guidance.

**19. Supply and administration of intranasal fentanyl spray in non-specialist palliative inpatient settings**

The Chairman welcomed Dr Debbie Jenkins, Palliative Care Consultant and Mrs Jane Barnes, Pharmacy Manager in Neville Hall Hospital to present the template for the supply and administration of intranasal fentanyl spray as an exemplar of good practice for adaption for use within NHS Wales. Dr Jenkins clarified the purpose of the protocol - to facilitate the self administration of intranasal fentanyl preparations for patients who are admitted to non specialist palliative in-patient settings within Aneurin Bevan Health Board. The protocol provides for the safe and legal storage, administration and monitoring of these products, improving patient access to prompt analgesia. Dr Jenkins explained that the protocol under consideration was approved by Aneurin Bevan Health Board in October 2012 and a pilot had subsequently been conducted in February 2013. The protocol describes the Aneurin Bevan Health Board process for the prescribing, storage and administration of intranasal fentanyl preparations. It also contains appendices which detail patient assessment and consent forms, self administration record charts and a patient information leaflet for patients who had been assessed as suitable for self administration.

The Chairman opened the discussion. Mr John Terry relayed the views of the All Wales Chief Pharmacists Committee in response to the proposal. These were noted as follows:

**Self Administration**

Although not all hospitals currently operate self administration systems, they are prepared to adopt policies from other Health Boards. There would be training needs for nursing, medical and pharmacy staff and based on previous experience there are concerns over the nursing resource available to operate the scheme on all wards. This includes management of security, the acute nature and high turnover of patients which could make this unsuitable on many wards. The presence of other high risk / vulnerable patients on the ward is another risk factor that should be considered.

### **Policies and Procedures**

The process requires agreement and sign off in each Health Board and therefore, may not be universally adopted, as it will be dependent on the assessment of risks identified in each organisation.

The policy only refers to intranasal fentanyl. Some Health Boards responded that this is rarely used in non specialist palliative care and only occasionally used by specialists. It has been suggested that protocols should be developed for using all types of opioids suitable for self administration for breakthrough pain.

### **Storage**

Concerns were raised on the security in general acute wards where controls may be more difficult to maintain, especially as this would be used in a smaller cohort of patients and nurses are less likely to be familiar with the processes.

In conclusion, the All Wales Chief Pharmacists Committee supported the principles of improving access to opioids for this group of patients as an exemplar of good practice that may be used to inform local implementation.

The Chairman confirmed AWMSG's endorsement of the proposal as a template for good practice to improve the patient experience and acknowledged the safety benefits. He thanked Dr Jenkins and Mrs Barnes for co-ordinating the project.

### **20. Date of next meeting:**

The Chairman confirmed the date of the next AWMSG meeting to be held in Cardiff on **Wednesday, 20<sup>th</sup> November 2013 commencing 9.30 am** and closed the meeting.