

<b>Enclosure No:</b>	<b>1/AWMSG/1211</b>
<b>Agenda Item No:</b>	<b>5 – Minutes of previous meeting</b>
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## **ALL WALES MEDICINES STRATEGY GROUP**

### **MINUTES OF THE AWMSG MEETING HELD ON WEDNESDAY, 9<sup>th</sup> NOVEMBER 2011 COMMENCING 10.30 AM AT THE ANGEL HOTEL, ABERGAVENNY**

#### **MEMBERS PRESENT:**

**Did not  
participate in**

- |     |                       |  |             |
|-----|-----------------------|--|-------------|
| 1.  | Dr Bruce Ferguson     | Chairman   |             |
| 2.  | Dr Fraser Campbell    | GP with prescribing lead role                        |             |
| 3.  | Dr Geoffrey Carroll   | Welsh Health Specialised Services Committee          | <b>10</b>   |
| 4.  | Prof David Cohen      | Health Economist                                     |             |
| 5.  | Mrs Debbie Davies     | Representing other professions eligible to prescribe | <b>10</b>   |
| 6.  | Mr Stefan Fec         | Community Pharmacist                                 |             |
| 7.  | Dr Karen Fitzgerald   | Consultant in Pharmaceutical Public Health           |             |
| 8.  | Dr Stuart Linton      | Hospital Consultant                                  |             |
| 9.  | Mrs Susan Murphy      | Senior Primary Care Pharmacist                       |             |
| 10. | Mr Christopher Palmer | Lay member   |             |
| 11. | Ms Rebecca Richards   | Finance Director                                     |             |
| 12. | Mr Christian Smith    | Nurse Director                                       | <b>7, 8</b> |
| 13. | Mr Guy Thompson       | ABPI (Wales) representative                          | <b>8, 9</b> |
| 14. | Dr John Watkins       | Consultant in Public Health Medicine                 |             |
| 15. | Mr Roger Williams     | Senior Hospital Pharmacist                           | <b>10</b>   |

#### **IN ATTENDANCE:**

- |     |                      |                                   |  |
|-----|----------------------|-----------------------------------|--|
| 16. | Mr Alastair Meredith | Welsh Government                  |  |
| 17. | Dr Robert Bracchi    | NMG Chairman                      |  |
| 18. | Mrs Karen Samuels    | Welsh Medicines Partnership Board |  |
| 19. | Mrs Ruth Lang        | Welsh Medicines Partnership Board |  |

## 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
CHMP	Committee for Medicinal Products for Human Use
DH	Department of Health
EMA	European Medicines Agency
FAR	Final Appraisal Recommendation
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health Boards
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
WMP	Welsh Medicines Partnership

### 1. Welcome and introduction

The Chairman welcomed members. He confirmed that the quorum had been met and opened proceedings.

### 2. Apologies

Professor Philip Routledge  
Dr Philip Banfield (Dr Stuart Linton deputising)  
Dr Brian Hawkins (Mrs Susan Murphy deputising)  
Ms Ellen Lanham (Mr Stefan Fec deputising)  
Mrs Wendy Warren (Mr Christian Smith deputising)  
Dr Emma Mason (no deputy attending)

### 3. Declarations of interest

The Chairman asked members to declare any interests pertinent to the agenda. Mr Christian Smith declared a personal specific interest in relation to Jansenn-Cilag Limited and Pfizer Limited and it was confirmed he would be excluded from participating in appraisal 2 and 3. Mr Guy Thompson declared a personal non-specific interest in relation to appraisal 3 and 4, and the Chairman confirmed that Mr Thompson would be excluded from participating in these appraisals.

### 4. Chairman's report

The Chairman confirmed that on 1<sup>st</sup> November 2011 WMP had received official notification from David Haslam, Chairman of the NHS Evidence Advisory Committee that the Committee advised that the process used by the All Wales Medicines Strategy Group to produce Final Appraisal Recommendations had been accredited by NHS Evidence. Members were informed that accreditation is valid for three years from October 2011 and is retrospectively applicable to guidance produced using the processes described to the Committee by the Welsh Medicines Partnership. It was noted that all guidance produced following the accredited process from January 2011 is eligible to bear the NHS Evidence Accreditation Mark. It was confirmed that

the NHS Evidence Accreditation Scheme recognises organisations that demonstrate high standards in producing health or social care guidance and recommendations. The Chairman suggested that users of the accredited guidance can be confident in the quality of the information. It was confirmed that the process for accrediting producers of guidance and recommendations for practice is described on the website of NHS Evidence.

Members were informed that on Thursday, 20<sup>th</sup> October 2011, the AWMSG Steering Committee had considered Bristol Myers Squibb's request for an independent review of AWMSG's advice that dasatinib (Sprycel<sup>®</sup>▼) should not be recommended for use within NHS Wales for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive (Ph+) chronic myelogenous leukaemia in the chronic phase. The Chairman confirmed that the Steering Committee considered the grounds for this review had not been met and a detailed response to all the issues highlighted had been provided to the applicant company. It was confirmed that the FAR would be forwarded to Welsh Government for ratification.

The Chairman reported that representatives of the Welsh Medicines Partnership and the All Wales Medicines Strategy Group had attended the ABPI Cymru Wales annual lecture in the National Museum of Wales, Cardiff on Tuesday 1 November 2011 at which Lord Robert Winston presented a fresh look at human innovation and examined how advances in technology could shape our future. The Chairman thanked ABPI Wales and Cardiff University for hosting the prestigious event.

The Chairman announced that confirmation had been received of Welsh Government ratification of the following AWMSG recommendations:

Histamine dihydrochloride (Ceplene<sup>®</sup>▼) is not recommended for use within NHS Wales for maintenance therapy for adult patients with acute myeloid leukaemia in accordance with its licensed indication. The case for clinical effectiveness and cost effectiveness has not been proven.

Tenofovir disoproxil fumarate (Viread<sup>®</sup>▼) is recommended as an option for use within NHS Wales for the treatment of chronic hepatitis B (CHB) in adults with decompensated liver disease. Treatment should normally be initiated following dialogue with a specialist liver unit. AWMSG is of the opinion that tenofovir disoproxil fumarate (Viread<sup>®</sup>▼) is not suitable for shared care within NHS Wales for the above indication.

Members were informed that the following statements of advice, reported at the October meeting, had been ratified by Welsh Government.

Lapatinib (Tyverb<sup>®</sup>▼) cannot be endorsed for the treatment of patients with breast cancer, whose tumours over express 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

Abatacept (Orencia<sup>®</sup>▼) in combination with methotrexate cannot be endorsed for the treatment of moderate to severe active polyarticular juvenile idiopathic arthritis in paediatric patients 6 years of age and older who have had an insufficient response to other DMARDs including at least one TNF inhibitor

Adalimumab (Humira<sup>®</sup>▼) in combination with methotrexate cannot be endorsed for the treatment of active polyarticular juvenile idiopathic arthritis, in children and adolescents aged 4 to 17 years who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs

Azithromycin dihydrate (Azyter<sup>®</sup>▼) cannot be endorsed for local antibacterial treatment of conjunctivitis caused by susceptible strains: purulent bacterial conjunctivitis and trachomatous conjunctivitis caused by Chlamydia trachomatis

Sildenafil (Revatio<sup>®</sup>▼) cannot be endorsed for the treatment of paediatric patients aged 1 year to 17 years old with pulmonary arterial hypertension

Fluorouracil/salicylic acid (Actikerall<sup>®</sup>) cannot be endorsed for the topical treatment of slightly palpable and/or moderately thick hyperkeratotic actinic keratosis (grade I/II) in immunocompetent adult patients.

Dexamethasone (Ozurdex<sup>®</sup>▼) cannot be endorsed for the treatment of adult patients with inflammation of the posterior segment of the eye presenting as non-infectious uveitis

Belatacept (Nulojix<sup>®</sup>▼) cannot be endorsed for the prophylaxis of graft rejection in adults receiving a renal transplant, in combination with corticosteroids and a mycophenolic acid

Mequitazine (Primalan<sup>®</sup>) cannot be endorsed for the treatment of allergic conditions such as hay fever, perennial rhinitis, urticaria, pruritis of allergic origin and allergic reactions associated with insect bites and stings

Fondaparinux sodium (Arixtra<sup>®</sup>▼) cannot be endorsed for the treatment of adult patients with acute symptomatic spontaneous superficial vein thrombosis of the lower limbs without concomitant deep-vein thrombosis

The Chairman confirmed that in the absence of a submission from the holder of the marketing authorisation within the appropriate timescales, statements of advice are currently in preparation for the following:

Rifaximin (Xifaxanta<sup>®</sup>▼) for the treatment of travellers diarrhoea that is not associated with any of: fever, bloody diarrhoea, eight or more unformed stools in the previous 24 hours, occult blood or leucocytes in the stool

Calcium acetate/magnesium carbonate (Osvaren<sup>®</sup>) for the treatment of hyperphosphatemia associated with chronic renal insufficiency in patients undergoing dialysis (haemodialysis, peritoneal dialysis)

Ciprofloxacin (Cetraxal<sup>®</sup>) for the treatment of acute otitis externa due to susceptible isolates of Pseudomonas aeruginosa or Staphylococcus aureus

Digoxin immune fab (DigiFab<sup>®</sup>) for the treatment of known or strongly suspected, life-threatening or potentially life-threatening digoxin or digitoxin toxicity

Esomeprazole (Nexium<sup>®</sup> IV) for gastric antisecretory treatment, when the oral route is not possible, in paediatric patients aged 1 to 18 years of age

Nomegestrol acetate/estradiol (Zoely<sup>®</sup>) for oral contraception

Epoetin zeta (Retacrit<sup>®</sup>▼) for the reduction of exposure to allogeneic blood transfusions in adult non-iron deficient patients prior to major elective orthopaedic surgery, having a high perceived risk for transfusion complications

The Chairman announced the appraisals scheduled for the next meeting on Wednesday, 7<sup>th</sup> December 2011. The Chairman clarified that as these appraisals form part of a pilot for appraising medicines in line with the limited submission process, detailed discussion is not

anticipated. The Chairman confirmed that applicant companies would be invited to attend and, in line with the appraisal process for full submissions, opportunity would be extended to all members and companies to raise any outstanding issues.

Appraisal 1: Alteplase (Actilyse® 2 mg Cathflo) thrombolytic treatment of occluded central venous access devices including those used for haemodialysis

Applicant Company: Boehringer Ingelheim Ltd

Appraisal 2: Saxagliptin (Onglyza®▼) as an add-on combination therapy for use in adult patients with type 2 diabetes mellitus with moderate or severe renal impairment to improve glycaemic control

Applicant Company: Bristol-Myers Squibb/AstraZeneca EEIG

Appraisal 3: Sodium valproate (Episenta®) for the treatment of manic episode in bipolar disorder when lithium is contraindicated or not tolerated. In patients who respond, consider continuation of treatment

Applicant Company: Beacon Pharmaceuticals Ltd

The Chairman reminded members to declare any interest to WMP in relation to the appraisal scheduled. The Chairman invited patients, patient organisations and patient carers to submit their views and contact WMP for further information in relation to the future work programme.

## **5. Minutes of previous meeting**

The minutes of the previous meeting were checked for accuracy. There were no matters arising.

## **6. Appraisal 1 - Tapentadol prolonged release (Palexia SR®) for the management of severe chronic pain in adults, which can be adequately managed only with opioid analgesics**

The Chairman invited members to declare interests in either the applicant company or the medicine – there were none. Dr David Jarrom, WMP assessment lead, joined members.

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 officials, 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 reiterated that NMG had considered the clinical and cost effectiveness issues in detail and had taken account of medical expert and patient organisation views. Members were reminded not to repeat the detailed discussion held at NMG but to seek clarification of any outstanding issues in relation to clinical or cost-effectiveness, consider the company response to the preliminary recommendation and take into account societal and budget impact issues. He confirmed that members would retire to vote in private and agree the recommendation, which would be subsequently announced.

The Chairman welcomed delegates from the applicant company, Grunenthal Ltd.

The Chairman invited Dr Robert Bracchi, Chairman of the New Medicines Group, to provide an overview of the discussions held at the preliminary appraisal and set the clinical context of the appraisal. He relayed the views of NMG and the clinical experts, and confirmed that a patient organisation submission had been received from Arthritis Care in Wales and was considered by NMG. He relayed NMG's preliminary recommendation that tapentadol prolonged release (Palexia® SR▼) should be recommended as an option for restricted use within NHS Wales. NMG considered that tapentadol prolonged release (Palexia® SR▼) should be restricted for use

in patients in whom morphine sulphate modified release has failed to provide adequate pain control or is not tolerated for the management of severe chronic pain in adults, which can be adequately managed only with opioid analgesics. Members were informed that NMG were of the opinion that tapentadol prolonged release (Palexia® SR▼) should be initiated by a specialist; however prescribing could be continued in primary care with appropriate communication and specialist input.

The Chairman reiterated that members should only consider the evidence provided and should not take account of any potential future fluctuations in price.

The Chairman opened the discussion and invited members to highlight issues in relation to the case for clinical effectiveness. Members sought clarification of the management of constipation, anti-emetic use and the place of the medicine in therapy. It was confirmed that the medicine is a controlled drug. There was discussion around the sub-population and potential publishing of data from the KF12 study.

The Chairman invited Professor David Cohen to provide his views in relation to the case for cost effectiveness. Prof Cohen provided clarification of the cost utility analysis in the company's submission and provided a brief overview of the trials, studies and analyses undertaken and included in the case for cost effectiveness. Clarification was sought in relation to the drug cost in Table 1 and it was confirmed that the assumptions were applied uniformly.

The Chairman referred members to the clinical expert summary and the Welsh Medicines Partnership appraisal lead highlighted salient issues within the document. There were no broader societal or budget impact issues of note. The patient representative drew attention to the salient issues highlighted within the patient organisation submission. Members' attention was drawn to the company response to the preliminary recommendation, particularly in relation to the issue of specialist initiation. The company delegates questioned the requirement for specialist initiation.

The company delegates responded to the questions and were offered opportunity to highlight outstanding issues. The company delegates clarified the use of laxatives and anti-emetics compared to comparators within the meta analysis study. Members were informed that evidence from the KF12 Study had not been published and the applicant company had no plans to publish the data. The company delegates highlighted the response rates within the sub-population. There was discussion in relation to withdrawal rates. It was noted that Grunenthal Limited had welcomed NMG's positive preliminary recommendation and had confirmed there were no outstanding issues from their perspective.

Prior to concluding the appraisal, the Chairman asked the delegates from Grunenthal Limited to confirm that all the outstanding issues had been addressed and they agreed that the process had been fair and transparent. The Chairman thanked Grunenthal Limited for engaging in the appraisal process. Members were asked to make a note of their recommendation and the Chairman moved on to the second appraisal. Mr Christian Smith left the meeting.

### **Appraisal decision**

The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, AWMSG had come to the following decision:

**Tapentadol prolonged release (Palexia® SR▼) is recommended as an option for restricted use within NHS Wales, only in the following subpopulation within its licensed indication:**

- **Patients with severe chronic pain, in whom morphine sulphate modified release has failed to provide adequate pain control or is not tolerated.**

**Tapentadol prolonged release (Palexia® SR▼) is not recommended for the management**

**of severe chronic pain in adults, which can be adequately managed only with opioid analgesics, outside of the subpopulation described above.**

**AWMSG is of the opinion that tapentadol prolonged release (Palexia® SR▼) should be initially prescribed by a specialist\*. Prescribing may be continued in primary care with appropriate communication and specialist input.**

\*Specialist implies specialist team or GP with special interest (GPwSI) with appropriate accreditation from the specialist faculty.

- 7. Appraisal 2 - Paliperidone palmitate (Xeplion®▼) prolonged release suspension for injection for the maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone. In selected adult patients with schizophrenia and previous responsiveness to oral paliperidone or risperidone, it may be used without prior stabilisation with oral treatment if psychotic symptoms are mild to moderate and a long-acting injectable treatment is needed**

The Chairman invited members to declare interests in either the applicant company or the medicine if they had not already done so – there were no additional declarations. Mr Smith was not in attendance. Dr Claire Davis, WMP Appraisal Lead, joined members.

The Chairman welcomed delegates from the applicant company, Janssen-Cilag Limited.

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 officials, 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 Dr Robert Bracchi, Chairman of the New Medicines Group, to provide an overview of the discussions held at the preliminary appraisal and set the clinical context of the appraisal. Dr Bracchi informed members that NMG had considered that paliperidone palmitate (Xeplion®▼) prolonged release suspension for injection should not be recommended for use within NHS Wales for the maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone; or in selected adult patients with schizophrenia and previous responsiveness to oral paliperidone or risperidone, without prior stabilisation with oral treatment when psychotic symptoms are mild to moderate and a long-acting injectable treatment is needed. He highlighted the limitations of the submission and confirmed NMG had not considered that a cost minimisation analysis had been appropriate for this submission and had agreed that the case for cost effectiveness had not been proven. Dr Bracchi confirmed that patient organisation submissions from Hafal and SANE had been considered by NMG.

The Chairman opened the discussion and invited members to highlight issues in relation to the case for clinical effectiveness. Members sought clarification in relation to compliance, length of hospital stays, study powering and BMI levels.

The Chairman invited Professor David Cohen to provide his views in relation to the case for cost effectiveness. Professor Cohen confirmed that the cost minimisation analysis had assumed equivalence with the comparator. Professor Cohen highlighted salient issues within the cost effectiveness evidence submitted by the applicant company. Professor Cohen also alluded to the company response to the PAR.

Mrs Samuels highlighted the general principle that as part of the appraisal process applicant companies have opportunity to submit a response to the ASAR prior to the NMG meeting. Any

further comments or new information received after this stage would not have been assessed by WMP as part of the ASAR, or considered by the New Medicines Group.

The Chairman asked members to highlight outstanding issues in relation to the case for cost effectiveness. Clarification was sought in relation to hospitalisation costs and the difference between the two groups within the economic analysis. Clarity was sought regarding the measure of the clinical effectiveness in relation to length of stay in hospital. Dr Davis summarised the views of the clinical experts. There were no broader societal or budget impact issues of note. The patient representative drew attention to the main issues highlighted within the patient organisation submissions. It was noted that the patient organisations supported the availability of this medicine

The company delegates responded to members' questions and were offered opportunity to highlight any outstanding issues. Prior to concluding the appraisal, the Chairman asked the delegates from Jansenn-Cilag Limited to confirm that all the outstanding issues had been addressed and they agreed that the process had been fair and transparent. The Chairman thanked Jansenn-Cilag Limited for engaging in the appraisal process. The Chairman confirmed that members should make a note of their recommendation and proceeded to the next appraisal.

### **Appraisal decision**

The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, AWMSG had come to the following decision:

**Paliperidone palmitate (Xeplion<sup>®</sup>▼) prolonged release suspension for injection is not recommended for use within NHS Wales for the maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone; or in selected adult patients with schizophrenia and previous responsiveness to oral paliperidone or risperidone, without prior stabilisation with oral treatment when psychotic symptoms are mild to moderate and a long-acting injectable treatment is needed. The case for cost effectiveness has not been proven.**

### **8. Appraisal 3 - Collagenase clostridium histolyticum (Xiapex<sup>®</sup>) for the treatment of Dupuytren's contracture in adult patients with a palpable cord**

The Chairman invited members to declare interests in either the applicant company or the medicine that had not previously been declared. There were no additional declarations. Mr Smith and Mr Thompson were not in attendance. Mr Tony Williams, WMP Appraisal Lead, joined members.

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 officials, 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 reiterated that NMG had considered the clinical and cost effectiveness issues in detail and had taken account of medical expert and patient organisation views. Members were reminded not to repeat the detailed discussion held at NMG but to seek clarification of any outstanding issues in relation to clinical or cost-effectiveness, consider the company response to the preliminary recommendation and take into account societal and budget impact issues. He confirmed that members would retire to vote in private and agree the recommendation, which would be subsequently announced.

The Chairman welcomed delegates from the applicant company, Pfizer Limited.



The Chairman invited Dr Robert Bracchi, Chairman of the New Medicines Group, to provide an overview of the discussions held at the preliminary appraisal and set the clinical context of the appraisal. He relayed the views of NMG and the clinical experts, and confirmed that a patient organisation submission received from British Dupuytren's Society had been considered by NMG. Dr Bracchi relayed NMG's preliminary recommendation that collagenase *Clostridium histolyticum* (Xiapex<sup>®</sup>▼) should be recommended as an option for restricted use within NHS Wales for the treatment of Dupuytren's contracture in adult patients with a palpable cord. NMG considered that it should be restricted for use as an alternative to fasciectomy in a subset of adult patients with a total of two or less affected joints per hand where percutaneous needle fasciectomy is not appropriate, using up to three injections per joint, with no more than six injections per patient. Dr Bracchi relayed NMG's view that collagenase *Clostridium histolyticum* (Xiapex<sup>®</sup>▼) would not be suitable for shared care within NHS Wales for the above indication.

The Chairman opened the discussion and invited members to highlight issues in relation to the case for clinical effectiveness. Members sought clarification of the number of injections and adverse events.

The Chairman invited Professor David Cohen to provide his views in relation to the case for cost effectiveness. It was noted that a cost minimisation analysis had been provided and no head to head studies had been undertaken. The Chairman opened the discussion in relation to cost effectiveness. Members referred to the British Society Guidelines relating to the use of fasciectomy and sought clarification in relation to the thresholds for treatment.

The Chairman invited the WMP assessment lead to provide a summary of the clinical expert opinion. There were no broader societal issues or significant budget impact issues of note. The patient representative drew attention to the main issues highlighted within the patient organisation submission.

The Chairman invited Pfizer delegates to respond to the issues highlighted by AWMSG relating to adverse events, patient population and clinical pathway and potential training for prescribers. It was confirmed that Pfizer have a training regimen in place. The company delegates responded to all the questions and were offered opportunity to highlight outstanding issues. It was noted that Pfizer Limited had welcomed NMG's positive preliminary recommendation and had confirmed there were no outstanding issues from their perspective.

Prior to concluding the appraisal, the Chairman asked the delegates from Pfizer Limited to confirm that all the outstanding issues had been addressed and they agreed that the process had been fair and transparent. The Chairman thanked Pfizer Limited for engaging in the appraisal process. Members retired to vote.

### **Appraisal decision**

The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, AWMSG had come to the following decision:

**Collagenase *Clostridium histolyticum* (Xiapex<sup>®</sup>▼) is recommended as an option for restricted use within NHS Wales for the treatment of Dupuytren's contracture in adult patients with a palpable cord.**

**Collagenase *Clostridium histolyticum* (Xiapex<sup>®</sup>▼) should be restricted for use as an alternative to fasciectomy in a subset of adult patients with a total of two or less affected joints per hand where percutaneous needle fasciotomy is not appropriate, using up to three injections per cord, with no more than six injections per patient.**

**AWMSG is of the opinion that collagenase *Clostridium histolyticum* (Xiapex<sup>®</sup>▼) is not suitable for shared care within NHS Wales for the above indication.**

**9. Appraisal 4 - Rosuvastatin (Crestor®) for the prevention of major cardiovascular events in patients who are estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors**

The Chairman invited members to declare interests in either the applicant company or the medicine. There were no additional declarations. Mr Guy Thompson was not in attendance. Mr Tony Williams, WMP Appraisal Lead, joined members.

The Chairman welcomed delegates from the applicant company, AstraZeneca UK Limited.

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 officials, 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 reiterated that NMG had considered the clinical and cost effectiveness issues in detail and had taken account of medical expert and patient organisation views. Members were reminded not to repeat the detailed discussion held at NMG but to seek clarification of any outstanding issues in relation to clinical or cost-effectiveness, consider the company response to the preliminary recommendation and take into account societal and budget impact issues. He confirmed that members would retire to vote in private and agree the recommendation, which would be subsequently announced.

The Chairman invited Dr Robert Bracchi, Chairman of the New Medicines Group, to provide an overview of the discussions held at the preliminary appraisal and set the clinical context of the appraisal. Dr Bracchi relayed NMG's preliminary recommendation that rosuvastatin (Crestor®) should not be recommended for use in NHS Wales for the prevention of major cardiovascular events in patients who are estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors, and who are intolerant or contra-indicated to simvastatin. He outlined the reasons for this decision. Dr Bracchi confirmed that the view of the clinical experts had been considered by NMG. A patient organisation submission had not been received. It was noted that NMG had concerns in relation to long term safety. Dr Bracchi informed members that that no sub-group analysis had been provided for the sub-group highlighted by the applicant company and NMG had considered there was insufficient evidence for NMG to recommend its use.

The Chairman opened the discussion and invited members to highlight issues in relation to the case for clinical effectiveness. Clarification was sought in relation to the Framingham score and Jupiter study. The incidence and risk of diabetes was noted.

Professor David Cohen highlighted the salient issues relating to the case for cost effectiveness and then the Chairman opened the discussion to members. Clarification was sought in relation to compliance, list price and budget impact model. The Chairman invited the WMP lead assessor to provide a summary of the clinical expert opinion. There were no broader social or budget impact issues of note.

The Chairman referred members to the company response to the preliminary recommendation and invited comment. The company delegates were invited to respond to questions and issues highlighted in the discussion. Discussion points included extrapolation of the risk score model, end points, dose and transferability of results of studies in older populations to younger patients. In addition to responding to all the issues raised in the discussion, the company delegates were afforded opportunity to raise any other issues. In conclusion, the company

delegates provided a verbal account of the pertinent issues within their submission.

Prior to concluding the appraisal, the Chairman asked the delegates from AstraZeneca UK Limited to confirm that all the outstanding issues had been addressed and they agreed that the process had been fair and transparent. The Chairman thanked AstraZeneca UK Limited for engaging in the appraisal process. Members retired to vote.

### **Appraisal decision**

The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, AWMSG had come to the following decision:

**Rosuvastatin (Crestor®) is not recommended for use within NHS Wales for the prevention of major cardiovascular events in patients who are estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors. The clinical and cost effectiveness evidence provided was not sufficient for AWMSG to recommend its use.**

Following the announcement of the recommendation, the Chairman added that it was evident that the company were highlighting a sub-group - patients who were intolerant to simvastatin and atorvastatin - where the applicant company had considered the evidence was particularly advantageous. It was the view of AWMSG that insufficient evidence had been presented to examine this sub-group and, if this sub-group were to be re-examined, there would be a need for a new submission with evidence relating to this patient population.

The Chairman concluded the appraisal proceedings by confirming that the AWMSG recommendations would be forwarded by WMP to the applicant companies on or before Wednesday, 16<sup>th</sup> November 2011 and that the applicant companies had until Wednesday, 23<sup>rd</sup> November 2011 to accept the recommendation or lodge a request for an independent review, the grounds for which should be submitted to the Chairman in writing. It was confirmed the process would not be delayed if the applicant companies failed to respond to the deadline. It was stated that subject to receiving a request for an independent review within the appropriate timelines, the recommendations would be passed to Welsh Government officials on Thursday, 24<sup>th</sup> November 2011. The Chairman confirmed that the applicant companies would be informed when ratification had been received from Welsh Government.

The appraisal proceedings closed and Mrs Davies and Dr Carroll left the meeting.

## **10. All Wales Prescribing Advisory Group (AWPAG)**

Dr Lewis confirmed she had verbally presented the detail of the October AWPAG meeting at the previous AWMSG meeting. Clarification was sought in relation to the Gluten-free prescribing paper. Dr Lewis informed members that AWPAG had considered a briefing prepared by a T&FG of the NMMPB to address issues relating to the supply of gluten free products on prescription within NHS Wales. It was confirmed that AWPAG had supported the recommendations in the briefing and although it was intended that the briefing be presented to AWMSG for endorsement due to time constraints, this paper had been provided directly to the Chief Pharmaceutical Adviser. Clarification was sought in relation to erectile dysfunction and Dr Lewis confirmed that AWPAG would be considering this issue during the early part of next year. An update of the situation relating to Chloroprep was sought. Dr Lewis confirmed that the Chief Pharmaceutical Adviser would progress this issue within Welsh Government. It was noted that the AWPAG opinion was at variance to the advice in 1000 Lives.

### **Analgesics leaflet**

Dr Lewis referred members to a leaflet prepared by AWPAG to support the appropriate prescribing of analgesics. Dr Lewis informed members that AWPAG had been tasked with developing a patient leaflet as part of the invest-to-save initiative in relation to the prescribing of non-steroidal anti-inflammatory drugs (NSAIDs). She confirmed that since providing the leaflet

to members, a technical edit had been undertaken which had improved the consistency of the font size, amended a reference and addressed some typographic errors and colloquialisms. Dr Lewis clarified that if endorsed by AWMSG the leaflet would be placed on the AWMSG website as a downloadable document. There was a suggestion that 'elderly' be changed to 'older people' and another suggestion to include the effects on 'driving' within the document. There was general support for the document and acknowledgement that some of the technical jargon could be reviewed. In concluding the discussion, the Chairman confirmed AWMSG's endorsement in principle and suggested that it be reviewed in light of the comments regarding content.

#### **Dronedarone**

Dr Lewis informed members that AWPAG had reviewed the prescribing status of dronedarone and had recommended that dronedarone should be prescribed and monitored by specialist teams only. A national consultation in relation to a shared care protocol had been planned. At that stage there was engagement with the company who had input into the development of the shared care template. Dr Lewis reported that after reviewing the recent EMA statement, it was AWPAG's view that shared care would not be supported and a national consultation would no longer be appropriate. Dr Lewis confirmed she had been liaising with the Cardiologists and Chair of the Cardiovascular Society and, initially, the recommendation had been supported. Subsequently, reservations had been expressed that the smaller district general hospitals did not have the systems in place to support hospital only prescribing. The Chairman opened the discussion and there was general agreement that communication with tertiary centres would be required. The Chairman suggested that AWMSG might consider endorsement of the AWPAG recommendation and include a review date of one year when more data would be available, and the safety profile might be clearer. There was unanimous agreement to this approach.

- 11. The Chairman announced the date of the next AWMSG meeting on Wednesday, 7<sup>th</sup> December 2011 at The Angel Hotel, Abergavenny and closed proceedings.**