

<b>Enclosure No:</b>	<b>1/AWMSG/0415</b>
<b>Agenda Item No:</b>	<b>4 – 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 Wednesday,  
25<sup>th</sup> March 2015 commencing 9.30 am at [The  
Angel Hotel](#), Abergavenny, NP7 5EN**

**Did not  
participate in**

### **VOTING MEMBERS PRESENT:**

- |     |                       |   |       |
|-----|-----------------------|---|-------|
| 1.  | Dr Stuart Linton      | Chairman                                    |       |
| 2.  | Dr Geoffrey Carroll   | Welsh Health Specialised Services Committee |       |
| 3.  | Dr Catherine Bale     | Hospital Consultant                         |       |
| 4.  | Professor David Cohen | Health Economist                            |       |
| 5.  | Miss Anne Hinchliffe  | Public Health Wales                         |       |
| 6.  | Mr Stefan Fec         | Community Pharmacist                        |       |
| 7.  | Dr Emma Mason         | Clinical Pharmacologist                     | 11-14 |
| 8.  | Mrs Susan Murphy      | Managed Sector Primary Care Pharmacist      |       |
| 9.  | Mr Christopher Palmer | Lay Member                                  |       |
| 10. | Mr John Terry         | Managed Sector Secondary Care Pharmacist    |       |
| 11. | Mr Rob Thomas         | ABPI Cymru Wales                            |       |
| 12. | Dr Mark Walker        | Medical Director representative             |       |
| 14. | Mrs Louise Williams   | Nurse representative                        | 11-14 |
| 15. | Dr Bill Whitehead     | GP with Prescribing Lead role               |       |

### **IN ATTENDANCE:**

16. Mrs Karen Samuels, Head of HTA, AWTTTC
17. Dr Robert Bracchi, NMG Chairman
18. Ms Ruth Lang, Head of Liaison & Administration, AWTTTC

## **AWTTC APPRAISAL LEADS:**

19. Dr Claire Davis, Senior Appraisal Scientist
20. Dr Stephanie Francis, Senior Appraisal Scientist
21. Dr Caron Jones, Senior Appraisal Scientist
22. Mr Anthony Williams, Senior Appraisal Pharmacist / Team Leader

## **WELSH GOVERNMENT:**

Not represented.

## **List of Abbreviations:**

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

**1. Welcome and introduction**

The Chairman opened the meeting and welcomed members. He welcomed Dr Catherine Bale to her first AWMSG meeting as hospital consultant representative.

**2. Apologies**

Mr Alun Morgan (other professions eligible to prescribe)  
Dr Karen Fitzgerald (Miss Anne Hinchliffe attending)  
Mr Roger Williams (Mr John Terry attending)  
Professor Roger Walker (Chief Pharmaceutical Officer, Welsh Government)  
Professor John Watkins (AWMSG Vice Chair / Public Health Wales)  
Mr Stuart Davies (Finance Director representative)

**3. Declarations of interest**

The Chairman invited declarations of interest pertinent to the agenda. There were none.

**4. Minutes of previous meeting**

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

**5. Appraisal 1: Limited Submission (WPAS)**

**Dolutegravir/abacavir/lamivudine (Triumeq<sup>®</sup>▼)** for the treatment of human immunodeficiency virus (HIV) infected adults and adolescents above 12 years of age weighing at least 40 kg

The Chairman welcomed representation from the applicant company: ViiV Healthcare UK Ltd

The Chairman confirmed that appraisal 1 and 2 would be closed to members of the public because of the associated Welsh Patient Access Scheme containing commercially sensitive information.

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published. The Chairman outlined the sequence of events and invited Dr Stephanie Francis, AWTTTC assessment lead, to set the context of the appraisal.

Dr Francis presented an overview of the submission as detailed in the ASAR. Dr Francis confirmed that the application had been considered eligible for a limited submission because it was a significant new formulation of an existing medicine with a pro-rata or lower cost per treatment and the anticipated usage in NHS Wales was considered to be of minimal budgetary impact. She relayed the views of the clinical experts who highlighted the importance of having access to a variety of drugs so that clinicians can construct a treatment regimen suitable for the majority of patients. It was noted that Triumeq<sup>®</sup> offered a single tablet regimen for patients unable to tolerate tenofovir. Dr Francis relayed the expert's view that dolutegravir/abacavir/lamivudine (Triumeq<sup>®</sup>▼) would be appropriate for specialist only prescribing. Members were informed that a patient organisation questionnaire had been received from the Terrence Higgins Trust.

Dr Bracchi provided a brief overview of the relevant issues identified in the preliminary appraisal and confirmed NMG's decision that dolutegravir/abacavir/lamivudine (Triumeq<sup>®</sup>▼)

should be recommended as an option for use within NHS Wales for the treatment of Human Immunodeficiency Virus (HIV) infected adults and adolescents above 12 years of age weighing at least 40 kg. Dr Bracchi highlighted that the recommendation should only apply in circumstances where the approved Wales Patient Access Scheme is utilised.

The Chairman opened the discussion in relation to clinical effectiveness. Clarification was sought in relation to company's claim of statistical superiority. The Chairman drew attention to the clinical expert summary. There was discussion in relation to the estimated budget impact and number of patients eligible in Wales. The Chairman reminded members that no evidence of cost-effectiveness was required for a limited submission. Members were asked to consider wider societal aspects, and issues relating to pill burden were noted. The Chairman asked Mr Palmer to highlight relevant information from the patient organisation submissions. Mr Palmer relayed the organisation's comments - they welcomed this new treatment as an option for patients and recognized improvements in therapy for patients with the human immunodeficiency virus.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegate to comment. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal.

**Appraisal decision subsequently announced in public:**

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

**Dolutegravir/abacavir/lamivudine (Triumeq<sup>®</sup>) is recommended as an option for use within NHS Wales for the treatment of Human Immunodeficiency Virus (HIV) infected adults and adolescents above 12 years of age weighing at least 40 kg.**

**This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.**

**6. Appraisal 2 - Full Submission (WPAS)**

**Defibrotide (Defitelio<sup>®</sup>)** for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstructive syndrome (SOS) in haematopoietic stem-cell transplantation (HSCT) therapy in adults, adolescents, children and infants over one month of age

The Chairman welcomed delegates representing Jazz Pharmaceuticals Ltd.

The Chairman sought confirmation that there were no members of the public in attendance.

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published. The Chairman outlined the sequence of events and invited Mr Tony Williams, AWTTTC assessment lead, to set the context of the appraisal.

Mr Williams presented an overview of the submission as detailed in the ASAR and relayed the views of the clinical experts. Experts highlighted that veno-occlusive disease (VOD) of the liver is a rare, serious complication of chemotherapy and transplantation that is more frequently observed in the paediatric setting. The condition carries significant morbidity and high mortality; defibrotide (Defitelio<sup>®</sup>) is the only licensed treatment for this complication and, with treatment, patients would be less likely to require intensive care and/or die. It was the view of clinical experts that procuring the medicine for the prevention of VOD in high risk cases had been difficult. It was noted that use as a preventative strategy represented an unlicensed use that was not within the scope of the current appraisal. Mr Williams confirmed that a patient organisation questionnaire had been received from Myeloma UK.

The Chairman asked for the view of NMG. Dr Bracchi confirmed that NMG had been satisfied that the criteria for ultra orphan drug status had been met and the view of NMG was that defibrotide (Defitelio<sup>®</sup>▼) should be recommended for use within NHS Wales for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstructive syndrome (SOS) in haematopoietic stem-cell transplantation (HSCT) therapy. NMG considered that the recommendation should only apply in circumstances where the approved Wales Patient Access Scheme is utilised.

The Chairman opened the discussion in relation to clinical effectiveness. The company delegates explained the rationale for selecting historical control over best supportive care. Members asked whether quality of life or clinical outcome data was available in relation to the ten patients in Wales who had received this medicine on a compassionate basis. Members were informed that there is currently no obligation on clinicians to report on outcomes. The company delegates highlighted that information is being collected via the European Transplant Registry. There was discussion over the safety profile and rate of haemorrhage. Clarification was sought in relation to the dose. The Chairman referred to the clinical expert summary. There were no outstanding issues of note.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen confirmed his role as AWMSG health economist and confirmed he had no involvement in compiling the ASAR or in discussions at NMG. Professor Cohen summarised the strengths and key concerns in the case presented, as summarised in the ASAR by the AWTTTC health economist, and offered the company delegates opportunity to correct or comment on any aspect of his summary. The Chairman drew members' attention to the budget impact evidence in the ASAR. The projected uptake and the levels of uncertainty in the estimates were noted.

The Chairman invited Mr Chris Palmer to highlight the salient aspects of the patient organisation questionnaire submitted by Myeloma UK. The advantages to patients in improving quality of life and reducing the risk of death were noted. Myeloma UK urged AWMSG to approve the use of defibrotide within NHS Wales. There were no other societal issues of note.

The Chairman referred to the company response to the preliminary recommendation and invited the company delegates to highlight aspects of their response. Prior to concluding the appraisal proceedings he asked the company delegates to confirm they were satisfied that all issues had been adequately addressed and taken into account, and that the process had been fair and transparent. On receipt of this confirmation he concluded the appraisal proceedings.

#### **Appraisal decision subsequently announced in public:**

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

**Defibrotide (Defitelio<sup>®</sup>) is recommended for use within NHS Wales for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstructive syndrome (SOS) in haematopoietic stem-cell transplantation (HSCT) therapy.**

**This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.**

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

## **7. Chairman's report**

The Chairman opened the meeting to the public.

The Chairman confirmed that following the announcement in February 2015 of AWMSG's recommendation to Welsh Government in relation to aflibercept (Zaltrap<sup>®</sup>) in combination with irinotecan/5 fluorouracil/folinic acid (FOLFIRI) chemotherapy for the treatment of adults with metastatic colorectal cancer (MCRC) that is resistant to or has progressed after an oxaliplatin containing regimen, the applicant company, Sanofi-Aventis Limited, had requested an independent review. The Chairman informed members that he was considering the grounds and a response to this request would be forwarded to the applicant company over the next few days. Ratification of AWMSG's recommendations from the meeting held in February had been received and, with the exception of aflibercept, the final appraisal recommendations had been posted on the AWMSG website and the Service informed.

The Chairman informed members that staff of AWTTTC were working on the detail of AWMSG's new process for appraising orphan and ultra orphan medicines and would be sharing the document more widely via the TDA Partnership Group and AWMSG's patient and public involvement group. The Chairman confirmed that the appraisal by NMG of the first medicine in this pilot was due to be undertaken in April 2015. The Chairman announced that Dr Saad Al-Ismael had been appointed the new Chair of NMG. Dr Bracchi had been appointed Chairman of the new Clinical and Patient involvement Group (CAPIG). The Chairman thanked Dr Bracchi for his support of the AWMSG appraisal process.

The Chairman announced the appraisals scheduled for the next AWMSG meeting on Wednesday, 22<sup>nd</sup> April 2015 (in Cardiff) as follows:

### **Appraisal 1: Full Submission**

**Beclometasone dipropionate/formoterol fumarate (Fostair<sup>®</sup>)** for the symptomatic treatment of patients with COPD, with a FEV1 < 50% predicted normal (pre-bronchodilator) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators

**Applicant Company: Chiesi Ltd**

### **Appraisal 2: Full Submission**

**Ledipasvir/sofosbuvir (Harvoni<sup>®</sup>)** for the treatment of chronic hepatitis C in adults

**Applicant Company: Gilead Sciences Ltd**

### **Appraisal 3: Limited Submission**

**Adalimumab (Humira<sup>®</sup>)** for the treatment of active enthesitis-related arthritis in patients, 6 years of age and older, who have had an inadequate response to, or who are intolerant of, conventional therapy

**Applicant Company: AbbVie Ltd**

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

## 8. Appraisal 3: Full Submission

**Daclatasvir (Daklinza®)** in combination with other medicinal products for the treatment of chronic hepatitis C virus (HCV) infection in adults

The Chairman welcomed delegates representing Bristol-Myers Squibb Pharmaceuticals Ltd.

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman announced that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published. The Chairman outlined the sequence of events and invited Dr Claire Davis, AWTTTC assessment lead, to set the context of the appraisal.

Dr Davis presented an overview of the submission as detailed in the ASAR and relayed the views of clinical experts. Dr Davis highlighted the unmet need due to the significant number of patients infected with hepatitis C who are intolerant or ineligible for interferon treatment, including a significant number of patients that have been previously treated with interferon who have either relapsed or not responded. It was also highlighted that pegylated interferon and ribavirin is a relatively toxic treatment combination that is associated with significant number of adverse events, some of which are permanent. Dr Davis confirmed that a patient questionnaire had been received from the Hepatitis C Trust.

The Chairman asked Dr Bracchi to relay the views of NMG. Dr Bracchi informed members that the cost-effectiveness data presented in the company submission had not been sufficiently robust for NMG to recommend its use in the whole of the licensed population. Dr Bracchi confirmed NMG's decision that daclatasvir (Daklinza®) in combination with other medicinal products should be recommended as an option for restricted use within NHS Wales for the treatment of chronic hepatitis C virus (HCV) infection in adults. NMG considered that use should be restricted to patients with significant fibrosis (METAVIR score  $\geq$  F3) or compensated cirrhosis.

The Chairman invited comment in relation to the case for clinical-effectiveness. The intention to develop a national policy regarding use of new treatments for hepatitis C was noted. It was acknowledged that the policy would be influenced by the National Institute for Health and Care Excellence (NICE) recommendation for sofosbuvir and the affordability of these new treatments within NHS Wales which provide significant clinical advancement compared to previous therapies. Dr Davis highlighted the deferred funding arrangement in England in relation to sofosbuvir which had been granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; It was noted that implementation of the advice had been extended from three to six months. It was stated that the health technology may not be appropriately administered until certain health service infrastructure requirements including goods, materials or other facilities, or other appropriate health services resources, including staff are in place. It was acknowledged that a similar deferred implementation arrangement may need to apply in Wales. There was discussion in relation to disease prevalence and incidence. Dr Carroll confirmed the likely number of

patients in Wales that may meet the criteria for this treatment in combination with other medicinal products. Dr Carroll confirmed the involvement of Welsh Health Specialised Services Committee in developing a national access policy for Wales. The Chairman referred members to the clinical expert summary and sought confirmation from members that there were no further outstanding clinical issues for discussions before moving on to the case for cost-effectiveness.

The Chairman invited Professor Cohen to share his views in relation to the case for cost-effectiveness. Professor Cohen clarified his role as AWMSG health economist and summarised the key aspects of the case for cost-effectiveness outlined in the ASAR. He gave recognition to the strength of the company submission. He commented that the weaknesses were relatively minor. Members considered the projected budget impact and acknowledged the financial challenge to NHS Wales.

The Chairman asked Mr Chris Palmer to highlight salient aspects of the patient organisation questionnaire from Hepatitis C Trust. Mr Palmer relayed the view of the Trust that daclastavir represented a novel and major improvement in the treatment of chronic hepatitis C which would improve accessibility, tolerability and effectiveness, with no foreseeable disadvantages. Members sought clarification in relation to patient follow-up and review. The level of relapse was noted. Members acknowledged that the level of re-infection would impact on the cost-effectiveness. There were no other societal issues of note.

The Chairman referred members to the comprehensive response from Bristol-Myers Squibb Pharmaceuticals Limited and asked the delegates if they wished to provide any further comment. They had no comments. Prior to concluding the appraisal proceedings the Chairman asked the company delegates to confirm they were satisfied that all issues had been adequately addressed and taken into account, and that the process had been fair and transparent. On receipt of this confirmation he concluded the appraisal proceedings.

**Appraisal decision subsequently announced in public:**

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

**Daclatasvir (Daklinza<sup>®</sup>) in combination with other medicinal products is recommended as an option for restricted use within NHS Wales for the treatment of chronic hepatitis C virus (HCV) infection in adults. Use should be restricted to patients with significant fibrosis (METAVIR score  $\geq$  F3) or compensated cirrhosis. Daclatasvir (Daklinza<sup>®</sup>) in combination with other medicinal products is not recommended for use within NHS Wales outside of this subpopulation.**

**9. The role of Medication Safety Officers (MSO) and the process for implementation of Medication Safety Alerts in Wales**

The Chairman asked Mr John Terry to present Enc 5/AWMSG/0315 on behalf of Mr Roger Williams, Chair of the Pharmacists Quality and Patient Safety sub-group. Mr Terry explained the purpose of the paper - to provide details of the role of the MSO in Welsh Health Boards. He informed members that this new initiative links into the National Medication Safety network co-ordinated by NHS England. The paper outlines the structure required to support medication safety activities and the mechanism for the availability of medication safety notices and alerts in NHS Wales. Mr Terry summarised the background and explained that since the abolishment of the National Patient Safety Agency in 2012 there had been a gap in the mechanism for reviewing and implementing national medication safety issues within Wales. The proposal addressed this through a network of medication safety officers (MSOs) supported by appropriate infrastructure both within each health Board and nationally. The paper detailed requirements for:



- the proposed structure for MSOs within Wales
- the role of the MSO within the Health Board
- a new or existing medication safety committee within each Health Board
- the implementation of medication related patient safety alerts

Mr Terry asked AWMSG to endorse the following recommendations:

- That all Health Boards and Trust identify a post holder with responsibility for the role of MSO for the organisation. The individual will also participate in the MSO network activities
- That Health Boards and Trust ensure there is a medication safety committee in place to support the work of the MSO and medicines safety activities
- That Health Boards and Trust support the process for the implementation of medication related patient safety alerts

The Chairman opened discussion. There was general agreement that there is a need for local ownership and action. Clarification was sought in relation to the term of office and expertise of the health professional who may be appointed to the role of MSO. Mrs Williams commented that the MSO within Cardiff and Vale UHB is a pharmacist and an improvement at a local level had been identified within a relatively short period. Mr Terry confirmed that each organisation would take responsibility for appointing an individual appropriate to the role of MSO. Dr Bracchi confirmed that representatives from AWTTTC working within the Welsh National Poisons Unit and YCC Wales had recently met with the MSO Project Lead and had offered support to this initiative. Dr Mason highlighted the importance of communication and feedback with the reporter. Dr Whitehead reiterated the importance of identifying appropriate action where the harm occurs, particularly at GP practice and ward level. Mr Fec informed members that the current system within community pharmacy does not enable the reporter to identify themselves. The Chairman concluded the discussion by confirming AWMSG's unanimous support and endorsement of the recommendations.

#### **10. Prescribing Dilemmas: A Guide for Prescribers (document review)**

Dr Bracchi presented Enc 6/AWMSG/0315, an update of Prescribing Dilemmas. He explained that the document provided guidance for health professionals on prescribing situations not covered by NHS Wales, including private care and private prescriptions, travel, foodstuffs, infertility treatment, common ailments, complementary medicines and alternative therapies, erectile dysfunction, prescribing for self and family, visitors from overseas, unlicensed medicines, and prescribing outside national guidance. Dr Bracchi informed members that in light of discussion at the recent AWPAG meeting further changes were required to the reference section. The Chairman invited comment. Dr Whitehead raised an objection to the title of the document and suggested that prescribing guidance would be more appropriate. The Chairman explained that the document had been used as a valuable resource for a number of years and a change of name at this stage might cause confusion within the service. Several suggestions were noted:

- Page 5: final consultation – suggestion noted to include private dentists
- Page 7: medicines for unlicensed use – check requirement for written leaflet
- Page 10: fertility treatments - check change in shared care arrangements
- Page 11: sildenafil – suggestion to include 'must continue to endorse SLS'
- Provide clarity in relation to patient requests for change from a private prescription to a NHS prescription

Dr Bracchi agreed to update the document in light of comments received. The Chairman confirmed AWMSG support of the document.

## 11. **Appraisal 4: Limited Submission**

**Entecavir (Baraclude®)** for the treatment of chronic hepatitis B virus infection in nucleoside naive paediatric patients from 2 to < 18 years of age with compensated liver disease who have evidence of active viral replication and persistently elevated serum ALT levels, or histological evidence of moderate to severe inflammation and/or fibrosis

The Chairman welcomed delegates from Bristol-Myers Squibb Pharmaceuticals Ltd

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman referred to his previous statement that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published. The Chairman outlined the sequence of events and invited Dr Stephanie Francis, AWTTTC assessment lead, to set the context of the appraisal.

Dr Francis confirmed that the application had been considered suitable for a limited submission as it was a minor licence extension to an already established medicine. She provided an overview of the ASAR. It was noted that clinical experts suggested that entecavir was the preferred treatment option in children. It was noted that six patient organisations had been approached by AWTTTC; none had submitted views.

Dr Bracchi relayed the view of NMG that entecavir (Baraclude®) should be recommended as an option for use for the indication under consideration. The Chairman opened discussion in relation to clinical effectiveness. Clarification was sought in relation to treatment duration and response rates in paediatrics compared to adults. Company delegates confirmed that adherence is being monitored as part of a 5 year study which is currently on-going. The Chairman referred members to the budget impact estimates and there were no issues of note. There were no wider societal issues raised.

The Chairman referred to the applicant company's response to the preliminary recommendation and offered opportunity to the delegates to provide further comment. The Chairman sought and received confirmation from the applicant company delegates that the process had been fair and transparent, and all issues had been adequately addressed.

### **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:

**Entecavir (Baraclude®) is recommended as an option for use within NHS Wales for the treatment of chronic hepatitis B virus (HBV) infection in nucleoside naive paediatric patients from 2 to < 18 years of age with compensated liver disease who have evidence of active viral replication and persistently elevated serum alanine aminotransferase (ALT) levels, or histological evidence of moderate to severe inflammation and/or fibrosis.**

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to the relevant applicant company within five working days. He informed the delegates that they had had up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline

would not delay the process.

## 12. **Appraisal 5: Full Submission**

**Bedaquiline (Sirturo<sup>®</sup>▼)** for use as part of an appropriate combination regimen for pulmonary multidrug-resistant tuberculosis in adult patients when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability.

The Chairman welcomed delegates from Janssen-Cilag Ltd.

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chairman referred to the statement he made earlier that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published. The Chairman outlined the sequence of events and invited Dr Caron Jones, AWTTTC assessment lead, to set the context of the appraisal.

Dr Jones presented an overview of the submission as detailed in the ASAR. She relayed the views of the clinical experts that multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) are difficult conditions to treat and there is a high unmet need in terms of having effective agents available that can be used in combination with other medicines to successfully treat this condition. Dr Jones confirmed that two patient organisations had been contacted by AWTTTC but no questionnaires had been received. TB Alert UK had commented that “there is a desperate need for new drugs, both for shorter courses first line drugs, and for less toxic second line drugs, so bedaquiline and delamanid are important developments”. TB Alert UK also provided a useful patient story publication.

Dr Bracchi informed members that NMG considered bedaquiline (Sirturo<sup>®</sup>▼) satisfied the AWMSG criteria for ultra-orphan drug status and recommended the medicine should be available as an option for use within NHS Wales for the indication under consideration.

The Chairman opened discussion and invited comment in relation to the case for clinical effectiveness. Members considered the safety profile and clarification was sought in relation to patient deaths in the study. The applicant company delegates confirmed that no deaths were attributable to treatment. Members discussed the monitoring requirements and asked what commitment had been made to collect information on patient outcomes. Members were informed that the British Thoracic Society is in the process of setting up a Registry. The company delegates confirmed that, globally, Janssen-Cilag Ltd has a database and patient outcomes can be collated; they also highlighted a study currently ongoing which will collect safety and patient outcome information. Members were referred to the clinical expert summary and the views of clinical experts in Wales were noted.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen clarified his role as AWMSG Health Economist and explained that he had no involvement in the preparation of the ASAR, neither was he involved in discussions at NMG. He highlighted the key aspects of the case for cost-effectiveness identified within the ASAR and invited to respond to his synopsis. Members were asked to take into account the projected budget impact. There were no outstanding issues of note.

The Chairman referred to the applicant company’s response to the preliminary recommendation and offered opportunity to the delegates to provide further comment. Prior to

concluding the appraisal proceedings the Chairman asked the company delegates to confirm they were satisfied that all issues had been adequately addressed and taken into account, and that the process had been fair and transparent. On receipt of this confirmation he concluded the appraisal 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:

**Bedaquiline (Sirturo<sup>®</sup>) is recommended as an option for use within NHS Wales for use as part of an appropriate combination regimen for pulmonary multidrug-resistant tuberculosis in adult patients when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability.**

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

**13. Therapeutic Priorities and CEPP Summary 2015-2016**

The Chairman invited Mrs Kath Haines to present Enc 9/AWMSG/0315. Mrs Haines provided the background and summarised AWMSG's therapeutic priorities for 2015–2016. Members were informed that the priorities are identified according to the AWMSG Clinical Effectiveness Prescribing Programme (CEPP) framework for primary care which consists of two equally weighted elements - prescribing indicators and an educational component. The document also highlights opportunities within the General Medical Services (GMS) contract and resources that can be used to support local prescribing initiatives. Mrs Haines asked members to note the involvement of Audit Plus with regard to the anticoagulant national audit. The Chairman confirmed AWMSG's endorsement of the proposed therapeutic priorities and CEPP Summary for 2015-2016.

**14. NHS Wales prescribing analysis of tramadol (data to September 2014)**

The Chairman invited Mrs Kath Haines to present Enc 10/AWMSG/0315. Mrs Haines explained the purpose of the prescribing update is to keep health boards informed of any changes in prescribing since the tramadol educational resource materials were made available for use in NHS Wales in November 2013, and to benchmark current prescribing data with that of other health boards, England and NE England. The educational resource materials promote the appropriate prescribing of tramadol in NHS Wales. They are intended to raise awareness amongst healthcare professionals and patients of the potential harm associated with the misuse and diversion of tramadol, and to provide prescribers with information and training to aid the appropriate prescribing of tramadol as part of an overall pain management strategy. The materials include primary care, secondary care and emergency department audits, an educational slide set, bulletins, a patient information leaflet and a shared decision-making toolkit. These are available at [www.awmsg.com](http://www.awmsg.com). The document presented to AWMSG for information analyses tramadol prescribing data to September 2014 and highlights changes in prescribing since the publication of the educational materials.

The Chairman confirmed the date of the next meeting on **Wednesday, 22<sup>nd</sup> April at Cardiff Metropolitan University** and closed proceedings.