

Enclosure No:	1/AWMSG/0114
Agenda Item No:	5 – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

MINUTES OF THE AWMSG MEETING HELD ON WEDNESDAY, 20th NOVEMBER 2013 COMMENCING 9.30 AM AT CARDIFF METROPOLITAN UNIVERSITY, CYNCOED CAMPUS, CYNCOED ROAD, CARDIFF CF23 6XD

VOTING MEMBERS PRESENT:

**Did not
participate in**

- | | | | |
|-----|-----------------------|---|--------------|
| 1. | Prof Philip Routledge | Chairman | |
| 2. | Dr Fraser Campbell | GP with Prescribing Lead role | |
| 3. | Dr Geoffrey Carroll | Welsh Health Specialised Services Committee | |
| 4. | Mr Alan Clatworthy | Managed Sector Secondary Care Pharmacist | |
| 5. | Prof David Cohen | Health Economist | |
| 6. | Debbie Davies | Other professions eligible to prescribe | |
| 7. | Mr Stuart Davies | Finance Director | |
| 8. | Dr Karen Fitzgerald | Consultant in Pharmaceutical Public Health | |
| 9. | Dr Emma Mason | Clinical Pharmacologist | |
| 10. | Mrs Susan Murphy | Managed Sector Primary Care Pharmacist | |
| 11. | Mrs Ellen Lanham | Community Pharmacist | |
| 12. | Dr Stuart Linton | Hospital Consultant | |
| 13. | Mr Christopher Palmer | Lay Member | |
| 14. | Mr Lance Richards | ABPI Cymru Wales | 11-17 |
| 15. | Prof John Watkins | Public Health Wales | 12-17 |

IN ATTENDANCE:

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

ALL WALES THERAPEUTICS & TOXICOLOGY CENTRE (AWTTC) APPRAISAL LEADS:

19. Mrs Susan Cervetto, Senior Appraisal Pharmacist
20. Mrs Helen Adams, Senior Appraisal Pharmacist
21. Dr Claire Davis, Senior Appraisal Scientist

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
ECDF	English Cancer Drugs Fund
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 opened the meeting and welcomed Mr Alan Clatworthy to his first AWMSG meeting. He explained that Mr Clatworthy had been nominated to represent Managed Sector Secondary Care Pharmacists by the All Wales Chief Pharmacists, as both the member and deputy were unable to attend.

2. Apologies

Mr Roger Williams, Managed Sector Hospital Pharmacist
Mr John Terry, Managed Sector Hospital Pharmacist deputy
Professor Roger Walker, Chief Pharmaceutical Officer
Mr Christian Smith, Senior Nurse

Not in attendance

Dr Brendan Lloyd, Medical Director representative

3. Declarations of interest

The Chairman confirmed a non-personal, non-specific interest in Astra Zeneca in that a training

post within the Department of Pharmacology was part-funded by Astra Zeneca.

4. Minutes of previous meeting

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

5. Chairman's report

The Chairman informed members that Welsh Government ratification of AWMSG advice forwarded in October has not been received. The Chairman announced the publication of a Report for the Minister of Health and Social Care following a review of the appraisal of orphan and ultra-orphan medicines in Wales. The Chairman highlighted the deadline for comment was 23rd December and confirmed that AWMSG would be submitting a response by that date.

6. Tramadol Educational Resource Pack

The Chairman invited Miss Karen Jones and Mrs Kath Haines to present the educational resource materials produced by the All Wales Therapeutics & Toxicology Centre to support the appropriate prescribing of tramadol in NHS Wales.

Miss Jones explained the purpose was to raise prescribers' awareness of the risks of tramadol using data obtained from the National Poisons Information Service (NPIS) and Yellow Card Centre (YCC) Wales, to promote the appropriate prescribing of tramadol as part of an overall pain management strategy, to identify health boards with particularly high tramadol prescribing and to raise public awareness of the risk associated with long-term tramadol use, particularly people obtaining supplies through means other than prescription.

The Chairman opened the discussion and invited comment. Members went through the documentation and made some general comments which all broadly supported the work. There was discussion in relation to comparative safety data and it was suggested that its inclusion would provide more context. Concern was expressed over the potential to inadvertently divert prescribers to inappropriate alternative analgesics. The general issue of dealing with long term use of analgesia was discussed, and a suggestion was made to include a reference to the requirement for patients on long-term medication to inform the Driver & Vehicle Licensing Agency (DVLA). The inclusion of a secondary care audit was noted. Mrs Haines confirmed that WAPSU would be monitoring the basket of analgesia medications.

The Chairman closed the discussion by confirming AWMSG's endorsement of the educational initiative and thanked all who had contributed to the development of the resource pack.

7. 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

The Chairman welcomed representatives from the applicant company, Allergan 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 a statement, and confirmed it was 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. It was noted that botulinum toxin type A is already in routine clinical use, off label, across Wales. It was suggested that the impact of urinary incontinence reaches far beyond the physical symptoms and the use of Botox[®] may reduce the burden on carers leading to a positive societal benefit. The views of the clinical experts were relayed. Clinical experts confirmed that botulinum toxin type A has been a routine part of the clinical pathway for at least ten years and removal of this option would have a massive impact on a population of patients whose bladder problem is well controlled, as well as increasing the demand for, and use of, more invasive and expensive techniques including major reconstructive surgery. Members were informed that a patient organisation submission had been received from the MS Society Cymru.

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 botulinum toxin type A (Botox[®]) should be recommended as an option for use within NHS Wales 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.

The Chairman invited comment in relation to the case for clinical effectiveness. Members sought clarification in relation to long-term effects of use and explored the issue of collection of safety data.

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. It was noted that the applicant company had submitted a cost-utility model with best supportive care as the comparator. Professor Cohen highlighted his observations from the ASAR. The company delegates acknowledged the difficulty in estimating the number of patients in Wales and confirmed that clinical experts in Wales had suggested best supportive care would be the most appropriate comparator and long-term catheterisation had not been included. Professor Cohen highlighted the inconsistencies and was interrupted by the sounding of a fire alarm. The meeting was adjourned and the building evacuated.

When declared safe the meeting re-convened and appraisal proceedings continued. Professor Cohen confirmed his view that on balance the case for cost effectiveness had been made. Delegates of the applicant company commented that the summary presented by Professor Cohen had been very good.

The Chairman invited Mr Palmer to highlight salient issues within the patient organisation submission from the MS Society Cymru. Mr Palmer confirmed the MS Society's strong support for the introduction of Botox[®] as a treatment for urinary incontinence in people with MS in Wales. He highlighted the patient-reported evidence which overwhelmingly supported effectiveness in controlling the symptoms of urinary incontinence and improving quality of life. Mr Palmer relayed the view that Botox[®] meets an unmet clinical need for the indicated patient population and highlighted its advantages. Members sought clarification of the support provided by the applicant company in relation to training for clinicians. There were no outstanding broader societal issues of note. The Chairman drew members' attention to the projected budget impact.

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 Allergan 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:

Botulinum toxin type A (Botox[®]) is recommended as an option for use within NHS Wales 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.

8. Appraisal 2: 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

The Chairman welcomed representatives from the applicant company, Sanofi-Aventis 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 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 the views of the clinical experts were relayed. Clinical experts had suggested that since type 2 diabetes is a progressive disease, lifestyle modifications and mono and dual-therapies tend to fail, leading to the need for add-on treatments (triple-therapy) over time and this is the likely niche for which GPL-1 agonists should be recommended, consistent with NICE guidelines. One expert had expressed a preference to use liraglutide, and it was suggested that other clinicians would use exenatide prolonged release as a first-line therapy. Clinical experts highlighted a problem with both of these agents is that their licences for combination with insulin are either complicated or still awaited and, in this respect, lixisenatide would have an advantage. It was noted that the cheaper acquisition cost of lixisenatide might displace current GLP-1 agonists for first-line use, leaving them for escalation therapies for patients who do not hit glycaemic targets. It was also noted that lixisenatide is a once-daily GLP-1 agonist and will give choice in addition to liraglutide. Mrs Adams confirmed that no patient organisation submission had been received.

Dr Bracchi provided a brief overview of the issues highlighted at NMG and confirmed that NMG had agreed with the restriction suggested by the applicant company. Members were informed that NMG had a long discussion over the evidence of cost effectiveness. Dr Bracchi relayed the view of NMG that lixisenatide (Lyxumia[®]) should be restricted for use in the following circumstances within its licensed indication 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:

- In combination with basal insulin, with or without oral glucose-lowering medicinal products, in patients uncontrolled on basal insulin;
- In combination with oral glucose-lowering medicinal products in patients uncontrolled on two or more oral glucose-lowering medicinal products.

NMG considered that lixisenatide (Lyxumia[®]▼) should not be recommended for use within NHS Wales outside of these circumstances.

The Chairman opened the discussion. The company delegates were asked to clarify the rationale for the choice of indirect analyses conducted. Members were informed that the decision had been informed by the evidence available. There was discussion over the positioning dilemma of the medicine in relation to NICE clinical guidelines and the available evidence. The Chairman asked members if there were any outstanding issues in relation to the clinical expert summary. There were none.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen highlighted that the company had submitted a cost minimisation analysis as well as a cost utility analysis. He provided detailed explanation in relation to both models before summarising the key issues. The company delegates agreed with Professor Cohen's views and acknowledged the pragmatic approach suggested by Professor Cohen. Members were referred to the budget impact section of the ASAR.

Mr Palmer informed members of the attempts made by AWTTTC to identify a patient organisation submission. 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 Sanofi-Aventis Ltd for engaging in the appraisal process, concluded 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:

Lixisenatide (Lyxumia[®]▼) is recommended as an option for restricted use within NHS Wales.

Lixisenatide (Lyxumia[®]▼) should be restricted for use in the following circumstances within its licensed indication 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:

- In combination with basal insulin, with or without oral glucose-lowering medicinal products, in patients uncontrolled on basal insulin;
- In combination with oral glucose-lowering medicinal products in patients uncontrolled on two or more oral glucose-lowering medicinal products.

Lixisenatide (Lyxumia[®]▼) is not recommended for use within NHS Wales outside of these circumstances.

9. Proposals to address the implications to NHS Wales of the Cancer Drugs Fund in England

The Chairman invited Mrs Karen Samuels to introduce Enc 5/AWMSG/1113 a proposal to address the implications to NHS Wales of the Cancer Drugs Fund (CDF) in England. Mrs Samuels provided the background and explained that the CDF was introduced in England in 2010 and was set to run until March 2014. It was established in order to provide a means by which patients in England can access cancer medicines not routinely available on the NHS. On 1st April 2013, NHS England took over the responsibility for the operational management of the CDF. In September 2013 it was announced that this fund would continue beyond 2014. Welsh Government has rejected the setting up of a Cancer Drugs Fund in Wales on the basis that it would create unacceptable inequities between patients with cancer or with other serious or life-threatening conditions. Mrs Samuels suggested the challenge for NHS Wales is to ensure that the service meets the needs of the majority of the population, whilst still being able to address the particular needs of individual patients. It was suggested that a comprehensive and tailored range of policies and processes is therefore necessary to ensure that patients in Wales can access appropriate clinically effective and cost-effective medicines in a transparent, timely, fair and consistent manner. Members were informed of the need within NHS Wales to provide clarity in relation to access to medicines in certain scenarios which have occurred in relation the Cancer Drugs Fund in England. Three scenarios were highlighted and potential approaches to them identified.

1. When the anticancer medicine has been appraised by the National Institute for Health & Care Excellence (NICE), but NOT RECOMMENDED for use, and is available via the Cancer Drugs Fund in England.

NICE produce guidance on new licensed medicines which is applicable within England and Wales. Final NICE advice supersedes that of AWMSG. Appraisal by NICE takes account of the clinical effectiveness and the cost effectiveness of a medicine. If a medicine is made available via the English cancer drugs fund (ECDF), it is potentially available via this mechanism to patients in England but not patients in Wales.

Proposed approach

If a new anticancer medicine is not recommended for use by NICE on the grounds of lack of cost-effectiveness and then is made available via the ECDF in England, the manufacturer may wish to engage subsequently with AWMSG. The application (which would always be accompanied by an approved Wales Patient Access scheme [WPAS]) could, for example allow manufacturers to introduce evidence of wider societal benefit or to provide specific sub-population evidence as provided for by the AWMSG assessment process. It might also provide data reflecting specific cancer prevalence or particular service configuration differences in Wales.

2. When a submission has been requested for the anticancer medicine, but the licence holder has not provided evidence for appraisal by AWMSG and the medicine is not on the NICE work programme.

There have been occasions when, for a variety of reasons, the holder of the marketing authorisation has been reluctant to engage in the AWMSG appraisal process. It may be due to the very rare nature of the disease, in that the number of patients expected to receive the medicine in Wales is very small. It may be that the company considers the evidence is insufficient to gain a positive outcome. In the absence of engagement by the pharmaceutical company, a Statement of Advice is presently issued (which is subsequently endorsed by Welsh Government and posted on the AWMSG website). The statement is provided for information to NHS Wales and confirms that the Minister for Health and Social Services has ratified that the medicine "cannot be endorsed for use and, therefore, the medicine is not funded routinely within NHS Wales.

Proposed approach

If an anticancer medicine is available via the CDF in England, but has not been appraised by NICE and meets the criteria for appraisal by AWMSG, and the manufacturer will not engage with AWMSG to appraise the medicine, the cancer service in Wales will be consulted. Based on the views of the service and the strength of support in relation to the availability of the medicine, Welsh Government officials may wish to instruct AWMSG to appraise using publicly available information. The licence holder will be informed that an instruction to appraise has been received – this will be a final opportunity to reconsider engaging in the appraisal process. It should be noted that the option of Welsh Government instructing an appraisal using publicly available information on any medicine has been available since the inception of AWMSG, but has only rarely been used.

3. When an unlicensed medicine or a medicine for an unlicensed indication is available via the Cancer Drugs Fund in England.

There may be clinical situations when the use of an unlicensed medicine or use of a medicine outside the terms of the licence (i.e., 'off-label') may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence. Indeed several examples appear on the CDF list in England.

Proposed approach

A panel of clinical experts will be convened by the AWMSG Secretariat (The All Wales Therapeutics & Toxicology Centre-AWTTC) to assess the evidence of clinical and (whenever possible) cost-effectiveness of the anticancer medicine being used unlicensed/ off-label and available through the CDF for a particular indication, and an evidence summary will be issued to health boards. Membership of the panel will include cancer specialists and a health economist in addition to AWTTTC personnel.

The Chairman opened the discussion. There was general agreement amongst members that the approach should be extended to all treatment areas where alternative routes of commissioning exist in England, and should not be restricted to cancer medicines. The Chairman reiterated the urgency to immediately address equity issues specifically relating to the medicines on the ECDF and suggested that a move towards a similar approach for other therapeutics areas could follow. It was acknowledged that the proposal was a first step in addressing the challenges, some of which are currently outside the remit of AWMSG. There was a suggestion that a fourth scenario should be included – that of reprioritisation of the treatment. It was suggested that the reference to wider societal benefits/subpopulations (1) was misleading in that wider societal benefits/subpopulation are currently considered as part of the existing AWMSG process and AWTTTC are not proposing a new process which this statement implies. It was agreed this wording would be removed.

There was a general consensus that AWMSG should review the Exclusion Criteria in relation to anticipated publication of NICE guidance. It was suggested that the pharmaceutical industry could be encouraged to engage with AWMSG 'simultaneously to' NICE, as well as 'in advance of' a NICE submission. Members acknowledged problems in NHS Wales when a licence has been granted but national guidance is awaited.

Mrs Samuels highlighted that the approach outlined in point 2 is currently not restricted to cancer medicines and reiterated that Welsh Government reserves the right to instruct AWMSG to appraise a medicine in circumstances where the holder of the marketing authorisation has declined to engage in the AWMSG appraisal process. The Chairman confirmed that on behalf of AWMSG, AWTTTC will be exploring opportunities to improve links with IPFR panels in Wales and this work formed part of the recommendations of the Review of AWMSG's policy for appraising orphan and ultra orphan medicines. Reference was made to the response received from the Rarer Cancers Foundation which had been circulated to members for information prior to the meeting. The Chairman also highlighted the response received from Sanofi which had been circulated to all members for information prior to the meeting. The Chairman assured members that comments from all stakeholders were encouraged and would be taken into

account when moving forward the proposals.

Representatives from WHSSC outlined the dilemma of making value judgements in relation to very expensive medicines for very small numbers of patients, particularly in circumstances when specialist expertise and scientific evidence was unavailable within NHS Wales. It was reiterated that advice in relation to unlicensed medicines would not be issued via AWMSG; but would remain a health board decision based on available evidence. The positive feedback received in relation to previous evidence status reports produced by AWTTTC for health boards when making individual decisions was highlighted. Clarification was sought in relation to the proposed panel membership and the role of AWTTTC. There was a consensus that in the wider context membership of such a panel should include clinicians from a range of therapeutic areas and should not be restricted to cancer clinicians.

In concluding the discussion and endorsing the approach, it was agreed that AWTTTC would progress with tackling the inequities in relation to cancer medicines and consider a way forward to address the wider context in relation to equitable access for all therapeutic areas and would report back to AWMSG in the New Year.

10. Appraisal 3: 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

The Chairman welcomed the representative from the applicant company, 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. There were none.

The Chairman alluded to the statement pertinent to all appraisals and confirmed the application made for this medicine had been accepted as a limited submission. He explained that evidence of budgetary impact in comparison to the existing comparator product/s should be demonstrated. The Chairman confirmed that monitoring of the budget impact would be essential, and AWMSG reserved the right to request a full submission if the budget impact exceeded that estimated in the submission. He set the context of the appraisal and confirmed that the company delegates would be invited to respond to any issues raised.

The Chairman invited Mrs Susan Cervetto, AWTTTC assessment lead, to set the context of the appraisal. Mrs Cervetto presented an overview of the submission as detailed in the ASAR. Members were informed that clinical experts and patient organisations had declined the opportunity to submit their views in relation to this submission.

The Chairman invited Dr Bracchi, NMG Chairman, to give an overview of the relevant issues identified in the preliminary appraisal. Dr Bracchi confirmed that NMG had been concerned over the lack of clinical expert views. He relayed NMG's preliminary recommendation that etravirine (Intelence[®]▼) should be recommended as an option for use within NHS Wales, 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.

The Chairman opened discussion and invited comment. It was noted that three patient organisations had been approached by AWTTTC. There were no issues of note.

The Chairman referred to the applicant company response to the preliminary recommendation and offered opportunity to the delegate to highlight salient issues. Prior to concluding the discussion, the Chairman sought confirmation from the company delegate that the process had

been fair and transparent. He thanked Janssen-Cilag 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:

Etravirine (Intelence[®]) is recommended as an option for use within NHS Wales, 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.

Mr Lance Richards, ABPI Cymru Wales representative, left the meeting.

11. Appraisal 4: 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

The Chairman welcomed representatives from the applicant companies, Bristol-Myers Squibb UK and AstraZeneca Ltd. In light of the Chairman's declaration of a non-personal non-specific interest in Astra Zeneca confirmation was sought from members and the applicant company delegates that it was acceptable for him to chair the appraisal but would not vote. This was accepted. There were no other declarations of interests in either the applicant company or the medicine.

The Chairman alluded to his previous statement and confirmed the application made for this medicine had been accepted as a limited submission. He explained that evidence of budgetary impact in comparison to the existing comparator product/s should be demonstrated. The Chairman confirmed that monitoring of the budget impact would be essential, and AWMSG reserved the right to request a full submission if the budget impact exceeded that estimated in the submission. He set the context of the appraisal and confirmed that the company delegates would be invited to respond to any issues raised.

Dr Claire Davis, AWTTTC assessment lead, set the context of the appraisal and highlighted relevant aspects of the ASAR. She confirmed that a patient submission had been received from Diabetes UK (Cymru). Clinical experts had provided a view that type 2 diabetes is a progressive disease, leading to the need for add-on treatments (such as triple therapy) over time. The clinical experts highlighted that prevalence of diabetes in adults is expected to rise. It was noted that saxagliptin can be used in patients with mild to moderate renal impairment, a common problem in the elderly population. Dr Davis confirmed that the applicant company did not anticipate that saxagliptin would be supplied by a home healthcare provider.

Dr Bracchi relayed the view of NMG that saxagliptin (Onglyza[®]) should be recommended as an option for use within NHS Wales for the treatment of 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.

The Chairman invited members to highlight any outstanding issues in relation to clinical effectiveness. There were no issues of note. Members were referred to the patient organisation submission from Diabetes UK (Cymru). Mr Palmer highlighted the advantages from a patient perspective. It was noted that weight gain appears not to be an issues for the majority of

patients using the medication. Other advantages highlighted included reduced incidence of hypoglycaemia when used in combination, increased flexibility in treatment and simple dosing regimen. Disadvantages highlighted by Diabetes UK (Cymru) included potential side effects and hypoglycaemia when used in conjunction with certain other medicines. 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 Bristol Myers Squibb UK and AstraZeneca UK 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:

Saxagliptin (Onglyza[®]) is recommended as an option for use within NHS Wales for the treatment of 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.

12. Appraisal 5: 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). It is also indicated in patients with late-onset disease (partial enzyme deficiencies, presenting after the first month of life) who have a history of hyperammonaemic encephalopathy

It was announced that Lucane Pharma had declined the invitation to participate in the appraisal.

The Chairman alluded to his previous statement and confirmed it was pertinent to all appraisals.

Dr Claire Davis, AWTTTC assessment lead, set the context of the appraisal and presented an overview of the submission as detailed in the ASAR. Dr Davis confirmed that clinical experts had suggested that in addition to children, adults with these conditions are also treated with these medicines. Infants with very severe disease may die during their first hyperammonaemic episode, but a substantial proportion survive, and once diagnosed the prognosis is reasonably good with current ongoing care and prompt treatment of metabolic decompensations.

Dr Bracchi relayed the view of NMG that sodium phenylbutyrate (Pheburane[®]) should be recommended as an option for use within NHS Wales as 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). It is also indicated in patients with late-onset disease (partial enzyme deficiencies, presenting after the first month of life) who have a history of hyperammonaemic encephalopathy.

The Chairman invited members to consider the case for clinical effectiveness and highlight any outstanding issues in the submission. The Chairman referred members to the summary of clinical expert views and there were no issues of note.

The Chairman referred members to the patient organisation submission which had been received from families at Children Living with Inherited Metabolic Diseases (CLIMB). The Chairman asked Dr Davis to thank CLIMB for their valuable contribution which provided members with a very useful and practical insight into the condition. Mr Palmer highlighted salient aspects of the submission. There were no outstanding societal or budget impact issues of note. The Chairman drew attention to the applicant company response to the preliminary recommendation 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:

Sodium phenylbutyrate (Pheburane[®]) is recommended as an option for use within NHS Wales as adjunctive therapy in the chronic management of urea-cycle disorders, involving deficiencies of carbamylphosphate synthetase, ornithine transcarbamylase or argininosuccinate synthetase; 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.

13. 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

The Chairman welcomed delegates representing Pfizer Ltd. There were no declarations of interest.

The Chairman alluded to his previous statement and confirmed the application made for this medicine had been accepted as a limited submission. He explained that evidence of budgetary impact in comparison to the existing comparator product/s should be demonstrated. The Chairman confirmed that monitoring of the budget impact would be essential, and AWMSG reserved the right to request a full submission if the budget impact exceeded that estimated in the submission. He set the context of the appraisal and confirmed that the company delegates would be invited to respond to any issues raised.

Mrs Susan Cervetto, AWTTTC assessment lead, presented an overview of the submission as detailed in the ASAR. She relayed the comments of clinical experts that that etanercept is currently used off-licence to treat some children aged 2–4 years with polyarthritis or extended oligoarthritis, following failure of methotrexate and approval for use would: facilitate prescription, ensure patients were adequately treated and reassure patients' families. Children with psoriatic arthritis and enthesitis-related arthritis lack an approved disease modifying treatment after failure of methotrexate or sulfasalazine. Mrs Cervetto confirmed that a detailed patient organisation submission has been received from Arthritis Care in Wales. It was noted that etanercept (Enbrel[®]) will be supplied by a home healthcare provider.

Dr Bracchi confirmed NMG's preliminary recommendation that etanercept (Enbrel[®]) 10 mg (powder and solvent for solution for injection), 25 mg (powder and solvent for solution for injection and pre-filled syringe) and 50 mg (pre-filled syringe and pre-filled pen) should be

recommended for the treatment of:

- polyarthritis (rheumatoid factor positive or negative) in children aged 2 to < 4 years and extended oligoarthritis in children and adolescents ≥ 2 years who have had an inadequate response to, or who have proved intolerant of, methotrexate;
- psoriatic arthritis in adolescents ≥ 12 years who have had an inadequate response to, or who have proved intolerant of, methotrexate;
- enthesitis-related arthritis in adolescents ≥ 12 years who have had an inadequate response to, or who have proved intolerant of, conventional therapy.

The Chairman invited comment on the submission. Clarification was sought in relation to post marketing surveillance. The Chairman referred members to the summary of clinical expert views and there were no issues of note. There were no outstanding societal or budget impact issues of note.

It was confirmed that a patient organisation submission had been received prior to the AWMSG meeting from Arthritis Care in Wales. Mr Palmer referred members to the submission and relayed the organisation's strong support for an additional treatment option.

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 Pfizer 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:

Etanercept (Enbrel[®]) is recommended as an option for use within NHS Wales for the treatment of:

- **polyarthritis (rheumatoid factor positive or negative) in children aged 2 to < 4 years and extended oligoarthritis in children and adolescents ≥ 2 years who have had an inadequate response to, or who have proved intolerant of, methotrexate;**
- **psoriatic arthritis in adolescents ≥ 12 years who have had an inadequate response to, or who have proved intolerant of, methotrexate;**
- **enthesitis-related arthritis in adolescents ≥ 12 years who have had an inadequate response to, or who have proved intolerant of, conventional therapy.**

14. Proposal to adopt NICE commissioning advice on Highly Specialised Technologies within NHS Wales

The Chairman invited Mrs Karen Samuels, Head of HTA within AWTTTC, to provide an overview of Enc 10/AWMSG/1113. Mrs Samuels explained that AWTTTC had been requested to provide Welsh Government with a view on whether or not NHS Wales should adopt the commissioning advice issued by NICE in relation to Highly Specialised Technologies (HSTs). It was noted that in preparing the paper, AWTTTC was mindful of the pending outcome of the review of AWMSG's policy for appraising ultra orphan medicines and the potential impact the recommendations might have on the process for considering high cost medicines for patients with rare conditions. Mrs Samuels explained the background - in April 2013 the assessment of very high cost medicines for patients with rare conditions, previously undertaken by the Advisory Group for Specialised Services (AGNSS), had moved under the remit of NICE. Commissioning advice formerly issued by AGNSS was not applicable within NHS Wales. AWTTTC was asked to consider whether or not Wales should adopt the small number of final evaluation determinations anticipated to be issued by NICE in relation to highly specialised technologies. Mrs Samuels

confirmed the recommendation of AWTTTC was to support the adoption within NHS Wales of NICE guidance issued pending full review of the process when available.

The Chairman opened the discussion. Dr Geoffrey Carroll explained the background and informed members of his previous involvement in developing a framework for decision making for highly specialised medicines. Dr Carroll questioned the proposed approach and suggested that NHS Wales should consider whether the commissioning advice issued by NICE should be adopted but should also retain the option not to adopt it. Mr Stuart Davies agreed with Dr Carroll and expressed a reluctance to automatically adopt HST advice within NHS Wales given the differences in accountability. It was noted that some services are not available within NHS Wales and it was suggested that implementation can be a challenge due to the huge costs involved. It was noted that responsibility for commissioning advice would fall predominantly within WHSSC and closer alignment between AWMSG and WHSSC will be required.

In concluding discussions the Chairman confirmed AWMSG's acknowledgement of the importance of continuing to work closely with NICE to ensure alignment of processes, and confirmed the involvement of AWMSG in the continued development of NICE methodology for appraising highly specialised technologies. The Chairman confirmed AWMSG's support to fully engage with this development and consider the application of the NICE commissioning advice when clarity on its implementation within NHS Wales is available.

15. Proposal to adopt the principles of Value Based Assessment developed by NICE

Action for AWMSG:

The Chairman invited Dr Robert Bracchi to present Enc 11/AWMSG/1113 – AWTTTC proposal to adopt the principles of the value based assessment (VBA) process in Wales when appropriate and in light of the publication of final methodology by the National Institute of Health and Care Excellence (NICE). Mrs Samuels explained that AWTTTC had been requested by Welsh Government to prepare a paper proposing a way forward for NHS Wales in relation to Value Based Assessment. Members were informed of the background - in 2007 the Office of Fair Trading (OFT) had suggested Value Based Pricing (VBP) of branded medicines as a replacement for the Prescribing Price Regulation Scheme. It defined VBP as 'therapeutic value' and considered it best measured in terms of quality adjusted life years (QALY's). It proposed this method of assessment should be applied to all branded medicines. In June 2013 NICE accepted responsibility for progressing VBA. It was agreed that price negotiation would remain the responsibility of the Department of Health (DH). It is proposed that in January 2014 an interim scheme will be introduced by NICE. At the same time a consultation on the methodology will be undertaken. It is intended that the consultation period will be three months, and VBA will be introduced in September 2014. It should be noted that NHS Wales will have opportunity to input into the consultation.

It is anticipated that two major amendments to the current NICE methodology for assessing cost per QALY will be made:

1. The wider societal benefits (WSB) will be expanded beyond those falling on the NHS, e.g. costs to carers and employers.
2. Burden of illness (BOI) will reflect the severity of the illness. BOI takes into account quality of life and length of life.

Members were reminded that AWMSG had aligned its appraisal process closely with that of NICE's Technology Appraisals and prides itself on its close working relationship with NICE which has been helpful, particularly in developing the Welsh Patient Access Scheme. It was suggested that the AWMSG appraisal process should continue to work in partnership with NICE. Mrs Samuels confirmed AWTTTC's proposals that:

1. AWMSG should remain committed to and work in parallel with the NICE Health

Technology Appraisal Processes.

2. AWMSG should await the outcome of the NICE consultation on VBA and should consider the methodology before considering its implementation within Wales. On behalf of AWMSG, representatives of AWTTTC will continue to liaise closely with NICE and actively participate in VBA developments.
3. AWMSG should continue with the current health technology appraisal process, which takes account of wider societal benefits, until such time that detail regarding methodology becomes available.

The Chairman opened discussion and members expressed their views. There was a general consensus that as AWMSG's appraisal process was aligned to that of NICE it was important that the methodology was also in alignment. It was confirmed that a metric had been developed by NICE for the evaluation of societal benefits and burden of illness. In closing discussion the Chairman confirmed AWMSG's support of for AWTTTC exploring the continued alignment of this process.

16. Written evidence request by the National Assembly for Wales's Health and Social Care Committee - medical technologies

The Chairman confirmed that the National Assembly for Wales' Health & Social Care Committee had sought written evidence from AWMSG with regard to their enquiry in access to medical technologies. The Chairman referred members to Enc 12/AWMSG/113 – a draft response and invited comment. It was confirmed that WHSSC will also be responding to the consultation. There was general agreement that advice to NHS Wales should be based on evidence using a robust and transparent process. There was a suggestion to include continuous monitoring/measurement, an exit strategy, and to target groups who would gain most benefit. The Chairman agreed to take all the comments into consideration when forming his response on behalf of AWMSG.

17. AWMSG Constitution update (for information)

The Chairman confirmed that this had been withdrawn from the agenda pending further changes by Welsh Government.

18. The Chairman confirmed the date of the next AWMSG meeting: Wednesday 15th January 2014 in Abergavenny