Enclosure No:	**1/AWMSG/0518**
Agenda Item No:	**4** – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Draft minutes of the AWMSG meeting held Wednesday, 14th March 2018 commencing 9.30 am at the Park Inn Hotel, Cardiff North, Circle Way East, Llanedeyrn, Cardiff, CF23 9XF

VOTING MEMBERS PRESENT:

			Did not participate in
1.	Dr Stuart Linton	Chair & Hospital Consultant	
2.	Dr Jeremy Black	General Practitioner	
3.	Mr Stuart Davies	Finance Director	
4.	Prof Dyfrig Hughes	Health Economist	
5.	Mr Stefan Fec	Community Pharmacist	
6.	Prof Iolo Doull	Welsh Health Specialised Services Commission	
7.	Dr Balwinder Bajaj	Clinical Pharmacologist	
8.	Mrs Alison Hughes	Managed Sector Primary Care Pharmacist	
9.	Mr Bill Malcolm	ABPI Cymru Wales	
10.	Mr Chris Palmer	Lay Member	
11.	Dr Mark Walker	Medical Director	
12.	Mr John Terry	Managed Sector Secondary Care Pharmacist	
13.	Mrs Louise Williams	Senior Nurse	

IN ATTENDANCE:
Dr Saad Al-Ismail, NMG Chair
Dr Robert Bracchi, AWTTC Medical Adviser
Mrs Karen Samuels, Head of PAMS, AWTTC
Mrs Ruth Lang, Liaison Manager, AWTTC

AWTTC Leads:
Mrs Claire Thomas, WAPSU Pharmacist
Dr Claire Davis, Senior Scientist, AWTTC
Dr Stuart Keeping, Senior Scientist, AWTTC

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
ASAR	AWMSG Secretariat Assessment Report
AWMSG	All Wales Medicines Strategy Group
AWPAG	All Wales Prescribing Advisory Group
AWTTC	All Wales Therapeutics & Toxicology Centre
BMA	British Medical Association
CAPIG	Clinical and Patient Involvement Group
CEPP	Clinical Effectiveness Prescribing Programme
CHMP	Committee for Medicinal Products for Human Use
DoH	Department of Health
ECDF	English Cancer Drugs Fund
EMA	European Medicines Agency
EMIG	Ethical Medicines Industry Group
EOL	End of life
FAR	Final Appraisal Recommendation
FDA	US Food and Drug Administration
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health Board
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
NPI	National Prescribing Indicator
PAMS	Patient Access to Medicines Service
PAR	Preliminary Appraisal Recommendation
PAS	Patient Access Scheme
PPRS	Prescription Price Regulation Scheme
SMC	Scottish Medicines Consortium
SPC	Summary of Product Characteristics
TDAPG	Therapeutic Development Appraisal Partnership Group
T&FG	Task and Finish Group
UHB	University Health Board
WAPSU	Welsh Analytical Prescribing Support Unit
WCPPE	Welsh Centre for Pharmacy Postgraduate Education
WeMeReC	Welsh Medicines Resource Centre
WG	Welsh Government
WHO	World Health Organization
WHSSC	Welsh Health Specialised Services Committee
WPAS	Wales Patient Access Scheme

1. Welcome and introduction

The Chair opened the meeting and welcomed members. The Chair introduced Professor Iolo Doull who was attending his first meeting as WHSSC representative.

2. Apologies

Professor John Watkins, Public Health Wales
Dr Anwen Cope, representing other professions eligible to prescribe
Dr Emma Mason, Dr Balwinder Bajaj deputising
Dr Cath Bale & Dr Sue Jeffs, Hospital Consultant

3. Declarations of interest

Members were reminded to declare any interests. There were none.

4. Minutes of previous meeting

The draft minutes of the previous meeting were checked for accuracy and approved subject to the inclusion of an additional sentence confirming AWMSG's endorsement of the 2018-2019 National Prescribing Indicators.

Before opening the appraisal session the Chair reminded members that all appraisal questioning should fall within the appropriate scope and parameters for AWMSG decision-making.

Appraisal 1: Full Submission WPAS

5. Levodopa-carbidopa intestinal gel (Duodopa®) for the treatment of advanced levodopa-responsive Parkinson's disease with severe motor fluctuations and hyper-/dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results

The Chair confirmed that as the appraisal had an associated Wales Patient Access Scheme it would be undertaken in private to protect commercial confidentiality. The Chair referred members to the AWMSG policy for appraising orphan, ultra-orphan medicines and medicines developed specifically for rare diseases.

The Chair welcomed delegates from AbbVie Ltd and it was confirmed that individuals in the public gallery were staff of AWTTC and Welsh Government.

The Chair 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 Chair 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 Chair provided the context and reminded members that AWMSG had appraised Duodopa® in November 2017 and had not supported its use in NHS Wales. The marketing authorisation holder, AbbVie Ltd, appealed on the grounds of Process in that a Clinician and Patient Involvement Group (CAPIG) had not had opportunity to consider the medicine and explore the clinical and societal issues in more detail. The Chairman confirmed that he had agreed a CAPIG meeting should be convened and that AWMSG would reappraise the medicine to incorporate feedback from CAPIG. The CAPIG meeting took place on 24th January 2018. He invited the AWTTC appraisal lead to address the Group.

Dr Stuart Keeping, the AWTTC Appraisal Lead, provided an overview of the submission and relayed the key aspects of the ASAR. He confirmed that subsequent to the negative advice issued in 2007, the marketing authorisation holder had resubmitted new clinical evidence, a new

health economic model and an updated Wales Patient Access Scheme. The applicant company proposed that the appraisal should focus on use in a restricted subpopulation- for use in people who are not eligible for deep brain stimulation.

Dr Saad Al-Ismail confirmed that NMG had appraised levodopa-carbidopa intestinal gel (Duodopa®) on 4th October 2017 and supported its use for the treatment of advanced levodopa-responsive Parkinson's disease with severe motor fluctuations and hyper-/dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results. The view of NMG was that use of the medicine should be restricted to patients not eligible for deep brain stimulation and should not be used outside of this subpopulation. NMG considered that levodopa-carbidopa intestinal gel (Duodopa®) satisfied the AWMSG criteria for a medicine developed specifically for rare diseases as an ultra-orphan equivalent.

The Chair opened discussion in relation to clinical effectiveness. Clarification was sought in relation to the sustainability of benefits and the pooling of the clinical trial analyses. There was discussion in relation to the adverse event profile and quality of life studies. The Chair drew members' attention to the CAPIG summary and invited Dr Rob Bracchi to relay the issues. Dr Bracchi highlighted the impact of the effects of Parkinson's disease on patients, explaining the "off-periods", which patients experience. He highlighted that patients with advanced Parkinson's disease typically need 24/7 care. Dr Bracchi informed members that the three clinical experts who gave input at the CAPIG meeting had all treated patients with Duodopa®. The clinical experts described the patients' experiences. In particular, they emphasised that patients receiving Duodopa® had maintained their independence for longer and, without treatment, it was likely that these patients might have been admitted to a care or nursing home. It was noted that clinical experts considered that approximately 4-5 patients would be eligible for treatment with Duodopa® each year and they agreed that treatment should be restricted to those who cannot tolerate apomorphine or are not suitable for DBS (deep brain stimulation). The clinical experts had given assurances that strict access criteria would be applied and, subsequent to the CAPIG meeting, the Parkinson's Excellence Network (PEN) had developed suggested patient selection criteria for initiation and maintenance of Duodopa® therapy which had been submitted to AWMSG in advance of this meeting. Experts had informed CAPIG that although the proportion of adverse events was high they were due mainly to the percutaneous endoscopic gastrostomy needed for Duodopa® delivery. The adverse event profile was comparable to that experienced by other patients who required percutaneous endoscopic gastrostomy (i.e. for reasons other than Duodopa® treatment). Dr Bracchi relayed the views of clinicians that the 24 hour support helpline via Health Care at Home, the nurse support provided at the patient's home and the training and education of medical staff, were all highly valued services and released NHS medical care time, thus providing a significant financial benefit. Dr Bracchi highlighted that Wales is the only country in the UK where Duodopa® is not available to patients. Clinical experts at CAPIG had stated that access to treatment via the IPFR process had been time-consuming and caused unnecessary delays. It was suggested that the burden on the NHS and social care services could potentially be alleviated if patients were able to live at home for longer. Dr Bracchi highlighted that if recommended by AWMSG, NHS Wales could benefit from the financial savings offered via the Wales Patient Access Scheme. He made the point that NHS Wales is paying full list price when accessing the medicine via the IPFR process.

Mr Chris Palmer, relayed the key issues as outlined in the patient organisation submissions from Cure Parkinson's Trust and Parkinson's UK in Wales. He stated that Duodopa® offers patients an improved quality of life and an opportunity to live independently at home for longer. Carers can go back to work and the stress on family life is alleviated. Members were asked to note the importance of co-production and patient choice.

Professor Dyfrig Hughes provided an overview of the case for cost-effectiveness as outlined in the ASAR. He highlighted the limitations of the evidence. Members were referred to the estimates of budget impact and the number of patients eligible for treatment in Wales. The company delegates explained the rationale for their estimates. It was noted that there was no

breakdown of total lifetime costs. Professor Hughes made the point that increased use of cassettes would have a significant impact on the case for cost-effectiveness. Members discussed the long term efficacy, the range of QALYs and resulting differences in the incremental cost-effectiveness ratio (ICER). The Chair reminded members that a degree of latitude could be applied because of the equivalent orphan status of the medicine. The shelf-life of Duodopa® was discussed; the company confirmed that home care services assist patients with managing the storage of the treatment in their refrigerators.

The Chair referred to the response from AbbVie Ltd to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. The delegates drew members' attention to the small and significant patient group and high burden of care. They highlighted the burden on clinicians in applying for treatment via the IPFR process and the problem of delays in access for the patient. AWMSG was reassured that the financial savings to NHS Wales would be immediate from publication of positive advice and the company delegates confirmed that they did not envisage any increase in patient numbers. The delegates thanked AWMSG for the opportunity to input into the discussion and respond to questions.

In concluding, the Chair thanked the company delegates and, having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chair closed the appraisal.

The meeting was opened to the public

Appraisal decision subsequently announced in public:
The Chair 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:

Levodopa-carbidopa intestinal gel (Duodopa®) is recommended as an option for restricted use within NHS Wales.

Levodopa-carbidopa intestinal gel (Duodopa®) should be restricted for use in the following subpopulation within its licensed indication for the treatment of advanced levodopa-responsive Parkinson's disease with severe motor fluctuations and hyper-/dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results:

- **Patients not eligible for deep brain stimulation.**

Levodopa-carbidopa intestinal gel (Duodopa®) is not recommended for use within NHS Wales outside of this subpopulation.

This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

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

6. Chair's report

The Chair confirmed Welsh Government ratification of the following AWMSG advice:

Darunavir/cobicistat/emtricitabine/tenofovir alafenamide (Symtuza) is recommended as an option for use within NHS Wales for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and adolescents (aged 12 years and older with body weight at least 40 kg).

Lacosamide (Vimpat) is recommended as an option for use within NHS Wales as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in children from ≥4 years of age to ≤15 years of age with epilepsy.

Lopinavir/ritonavir (Kaletra) is recommended as an option for use within NHS Wales in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infected children aged from 14 days to less than 2 years old.

Rolapitant (Varuby) is not recommended for use within NHS Wales for the prevention of delayed nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy in adults. The case for cost-effectiveness has not been proven.

Members were informed that in the absence of a submission from the marketing authorisation holder, a statement of advice had been published to inform NHS Wales that Peginterferon alfa-2a (Pegasys) for the treatment of HBeAg-positive chronic hepatitis B in non-cirrhotic children and adolescents 3 years of age and older with evidence of viral replication and persistently elevated serum ALT levels cannot be endorsed for use.

The Chair informed members that Dr Saad Al-Ismail is retiring from the NHS and will be stepping down as Chair of the New Medicines Group. He thanked Dr Al-Ismail for his significant contribution to the work of NMG and AWMSG and wished him a long and healthy retirement.

The Chair confirmed that an independent review panel (IR) had been convened on 23rd January to explore concerns expressed by the marketing authorisation holder in relation to AWMSG's appraisal of afamelanotide (Scenesse®) for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria. The applicant company had requested an independent review, the grounds for which were based on dispute of scientific interpretation and process flaws. The Chair relayed the view of the panel that AWMSG had made a reasonable decision based on the data available and he confirmed that the panel were satisfied that due process had been followed. It was noted that the marketing authorisation holder, Clinuvel Pharmaceuticals Limited, had been informed that the complaints had not been upheld and that the initial recommendation would be forwarded to Welsh Government for ratification.

7. Therapeutic Priorities & CEPP Summary 2018-2019

The Chair requested members to consider the *Therapeutic Priorities and Clinical Effectiveness Prescribing Programme Summary 2018–2019* for endorsement. He explained the document had been developed to support health boards in the delivery of their CEPP programme. Claire Thomas presented a brief summary of the paper. The Chair opened discussion and asked members to suggest ways to support implementation. Members welcomed the document. There was a suggestion to develop the possibility of financial incentives for reinvestment from savings via the adoption of a whole system approach (for example across a disease area in primary and secondary care). The Chair acknowledged that AWMSG should consider different mechanisms for incentivising and it was suggested that tackling a disease area in this way might be a concept attracting wider clinical support. Members were reminded that the AWMSG Best Practice Day scheduled on 10th July would raise awareness of good prescribing practice and offer opportunity for local health boards to learn which initiatives have worked well in other areas. Mrs Thomas highlighted the SHARE platform hosted by AWTTC and invited health professionals to register for access to this communication tool to assist with communication between health boards and sharing of good practice. It was noted that the renegotiation of the GMS Contract might have an impact in the future with regard to the medicines management domain of the Quality and Outcomes Framework. The Chair closed discussion and confirmed AWMSG's strong support and endorsement of the document.

8. AWMSG Five Year Strategy 2018–2023

Dr Bracchi introduced the draft AWMSG Five Year Strategy 2018–2023 and confirmed that the document was being presented to AWMSG for endorsement. Dr Bracchi informed members that the strategy had been aligned with the recommendations of the 2018 Parliamentary Review of Health and

Social care in Wales - A revolution from within: transforming Health and Care in Wales. He confirmed the document had been shared with AWMSG members for discussion and comment on three occasions and had been sent out to stakeholders for consultation twice.

The Chair opened discussion. The need to measure value for money was raised and Dr Bracchi confirmed that further discussions would be had in relation to resource reallocation and thresholds for medicines appraisal. It was suggested that AWMSG should negotiate with manufacturers to ensure that NHS Wales was getting value for money. An example was shared of a high cost medicine that was being made available to patients living in England at a significantly reduced cost to that being offered to NHS Wales. The Chair confirmed the remit of AWMSG and explained that this would require constitutional change in its terms of reference. A suggestion was made that strengthening the executive function within Welsh Government might better control resource use. It was confirmed that AWTTC would arrange a separate meeting to discuss these issues in more detail. Mrs Samuels asked members to seek volunteers to lead on the recommendations. The Chair closed discussion and endorsed the AWMSG Strategy 2018-2013.

9. Appraisal 2: Full Submission

Misoprostol (Mysodelle®) for the induction of labour in women with an unfavourable cervix, from 36 weeks gestation, in whom induction is clinically indicated.

The Chair welcomed delegates from Ferring Pharmaceuticals (UK).

The Chair 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 Chair 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.

Dr Claire Davis, the AWTTC Appraisal Lead, set the context of the appraisal and relayed the key aspects of the resubmission as outlined in the ASAR. Members were informed that the resubmission included additional information to that previously appraised in 2016, i.e. a cost utility analysis and a patient preference survey.

Dr Saad Al-Ismail confirmed that NMG had appraised misoprostol (Mysodelle®) on 7th February 2018 and recommended it as an option for use within NHS Wales for the induction of labour in women with an unfavourable cervix, from 36 weeks gestation, in whom induction is clinically indicated**.**

The Chair opened discussion in relation to clinical effectiveness. Members sought clarification as to whether a shorter but more intensely painful labour might require additional supervisory support. The company delegates highlighted experience elsewhere in the UK that Mysodelle® had actually reduced the burden on the labour ward. It was noted that clinicians in Wales considered there was no unmet need in NHS Wales. Dr Davis highlighted that a leading maternity unit in the UK has been using Mysodelle® as the standard inpatient induction agent since December 2017. It is anticipated that the positive experience reported will result in a number of units following suit. It was noted that, as expected, a higher rate of hyperstimulation had been observed in the aforementioned maternity unit, but this was deemed to be easily managed with the removal of the pessary and the occasional use of terbutaline. Members discussed adverse reactions and it was highlighted that clinical experts do not consider Mysodelle® would be used in the out-patient setting due to the rapid onset of action and the higher rate of hyperstimulation. The issue of patient consent and the use of off-label prescribing for induction of labour was discussed.

The Chair referred to the patient organisation questionnaire submitted by the Birth Trauma Association. Mr Palmer highlighted that drugs which result in fast onset of labour and delivery often result in more psychological trauma which might need long term psychology treatment and cognitive behaviour therapy. Concerns in relation to uterine rupture and amniotic fluid embolism were also relayed; however it was noted that these adverse effects may not be specifically related to the drug. The company delegates reported that in the pivotal study, there were no reports of amniotic fluid embolism and only one report of uterine rupture, in a patient who already had scar tissue.

There was discussion in relation to the licensed indication as compared to that of the comparator, Propess®. It was noted that the medicine is available for use via health technology appraisal in Scotland for the indication under consideration. Members also discussed the patient preference survey and the limitations associated with it.

Professor Dyfrig Hughes provided an overview of the case for cost-effectiveness as outlined in the ASAR and highlighted the limitations. The Chair referred members to the budget impact estimates and it was noted that in all scenario analyses, the overall net budget impact remained cost saving with Mysodelle® when acquisition costs and resource savings are combined.

The Chair referred to the response from Ferring Pharmaceuticals (UK) to the preliminary recommendation and asked the delegates if they wished to make any closing remarks. The delegates thanked AWMSG for the opportunity to input into the discussion and respond to questions.

In concluding, the Chair thanked the company delegates and, having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chair closed the appraisal.

Appraisal decision subsequently announced in public:
The Chair 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:

Misoprostol (Mysodelle®) is recommended as an option for use within NHS Wales for the induction of labour in women with an unfavourable cervix, from 36 weeks gestation, in whom induction is clinically indicated.

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

The Chair confirmed the date of the next meeting on Wednesday, 18th April 2018 in Cardiff and closed the meeting.