

# BRITISH PHARMACOPOEIA COMMISSION

## Expert Advisory Group: Medicinal Chemicals 3

### SUMMARY MINUTES

A meeting of this Expert Advisory Group was held at 151 Buckingham Palace Road, London SW1W 9SZ on Wednesday 25<sup>th</sup> February 2015.

**Present:** Mr V Fenton-May (*Chairman*), Professor E Williamson (*Vice-chairman*), Professor M Almond, Mr S Arkle, Mr J Beach, Dr J Beaman, Mr C T Goddard, Mr P Hampshire, Dr K Pugh, Dr R Torano, Mr M Tubby and Mr I R Williams.

**In attendance:** Mr A Evans, Ms H Corns, Ms G Li-Ship and Ms C Pitt.

**Apologies:** Dr B Rackstraw.

### INTRODUCTORY REMARKS

The Chairman welcomed Mr Julian Beach and Dr Jon Beaman attending their first meeting as new members, also Ms Graziella Li-Ship and Ms Catherine Pitt from the Secretariat.

The Chairman reminded members that Mr Wayne Jeffries should be contacted if members experienced any difficulties with their travel bookings or expenses claims.

The Chairman reiterated to members the confidential nature of the papers presented at EAG meetings and that members should declare any interests at the start of each agenda item.

### I MINUTES

The minutes and summary minutes of the meeting held on 7<sup>th</sup> October 2014 were confirmed.

### II MATTERS ARISING FROM THE MINUTES

The following matters arising from the meeting held on 7<sup>th</sup> October 2014 were noted.

**The following had been completed for BP 2016:**

Non-interchangeability statements had been amended for the monographs highlighted by the anti-epileptic drugs review.

Extemporaneous formulations containing chloroform had been removed from monographs. The draft revised monograph for Dexamethasone Sodium Phosphate Injection had been amended as agreed at the last meeting and will be published.

**Alfacalcidol Capsules** Following an internal investigation, chloroform may be used as a reagent where a suitable/safer alternative could not be found.

**Spray reagents for TLC** Further discussions were to be held within BP Secretariat

**Acarbose Tablets** The draft monograph has been amended as agreed and circulated to both the USP and JP.

**Estradiol Vaginal Tablets** The monograph had been distributed for consultation.

**Cyproterone Tablets** The monograph had been distributed for consultation.

**The following draft monographs have been sent to the Laboratory for investigation:**

Dihydrocodeine preparations  
Alfacalcidol preparations  
Amitriptyline preparations  
Gestodene and Ethinylestradiol Tablets  
Ethinylestradiol Tablets

**Diazepam Preparations** Mr Hampshire has agreed to work with the BP Secretariat to investigate the methods in the draft monographs.

**Ergocalciferol /Colecalciferol Preparations** Mr Goddard had agreed to provide data, it was anticipated that revised draft monographs would be discussed at the next EAG meeting.

**III REPORTS AND CORRESPONDENCE**

**425 Emergency Procedure MC3(15)1**

The emergency procedure for 151 Buckingham Palace Road was provided.

**426 Members' details MC3(15)2**

Members were asked to check the circulated contact details and to inform the Secretariat of any amendments required.

**427 British Pharmacopoeia Chemical Reference Substances MC3(15)3**

The British Pharmacopoeia Chemical Reference Substances approved since the last meeting of the EAG were noted.

**428 EAG Work Programme MC3(15)4**

A copy of the work programme for EAG: MC3 was provided to members for information. Members were asked to contribute data should they have an interest in any of the products.

**429 BP Updates MC3(15)5**

The Secretariat provided members with an update on changes within the MHRA and the BP.

**430 Monographs for Omission MC3(15)6**

**Monograph omissions** The monographs highlighted at the last meeting of the group had been through the omissions process. Members agreed that the following monographs should be omitted from future publications of the BP:

Aminoglutethimide Tablets	Glucose Irrigation Solution
Amitriptyline Embonate	Halibut Liver Oil
Carbenoxolone Sodium	Halibut-Liver Oil Capsules
Codergocrine Tablets	Menadiol Phosphate Injection
Desipramine Tablets	Methylcellulose Granules
Diethylstilbestrol Pessaries	Morphine and Atropine Injection
Dydrogesterone Tablets	Nandrolone Phenylpropionate
Ergometrine Tablets	Nandrolone Phenylpropionate Injection
Fosfestrol Sodium (and IR spectra)	Paraffin Ointment
Fosfestrol Injection	Protriptyline Tablets
Fosfestrol Tablets	Tretinoin Solution
Fructose Infusion	

**Monograph responsibility changes** It was further agreed that the responsibility for the following monographs should be transferred to the EAG for unlicensed medicines:

Benzatropine Mesilate  
Benzatropine Injection  
Benzatropine Tablets  
Oxymetholone  
Oxymetholone Tablets

**Diethylstilbestrol Tablets** Members discussed a proposal to use an A(1%, 1 cm) value in the Assay to remove the need for the BP Laboratory to maintain the diethylstilbestrol BPCRS. This was considered, in theory, acceptable for the Assay, however, members agreed that this was a weakening of the monograph as the tests were all non-specific and the inclusion of the BPCRS was significant for the overall quality of the monograph. Members recommended the Secretariat identified means to strengthen the monograph in other areas before this proposal was taken forward.

**431 Dispensing and Supply Statements**

**MC3(15)7**

**Specific Monographs** Members agreed with the recommendations from EAG PCY to delete the Dispensing and Supply statements (when X is prescribed or demanded, Y shall be dispensed or supplied) in the following monographs:

Hypromellose Eye Drops  
Sodium Picosulfate Oral Solution  
Isosorbide Dinitrate Tablets  
Isosorbide Dinitrate Sublingual Tablets

**Neonatal Naloxone Injection** Members agreed that the monograph should be omitted and the Naloxone Injection monograph be amended to control all available strengths. The lower strength product was no longer named as Neonatal in practice and prescribed as Naloxone Injection with the lower strength included.

**Calciferol Prescribing Statement** The proposal to delete the statement regarding the dispensing and supply of colecalciferol (or ergocalciferol) was discussed. Members questioned the current statement "When calciferol formulation is prescribed or demanded, Colecalciferol formulation or Ergocalciferol formulation shall be dispensed or supplied" as the two products to supply were different. EAG PCY would be asked which product should be supplied when calciferol was requested and if a synonym should be added to the monographs.

**Dispensing statements in the BP** Experts agreed that the BP should not be used as a prescribing reference manual and recommended that EAG PCY continued to review these statements with a view to omitting them where possible.

**432 Injection Characteristics**

**MC3(15)8**

Members agreed to delete the Characteristics section in the following monographs as these were not of value to the user and, in some cases, were not in agreement with licensed specifications:

Hydrocortisone Acetate Injection;  
Methylprednisolone Acetate Injection;  
Triamcinolone Acetonide Injection.

#### **IV NEW MONOGRAPHS**

**433 Desogestrel and Ethinylestradiol Tablets MC3(15)9**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

**434 Raloxifene Tablets MC3(15)10**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

**435 Testosterone Gel MC3(15)11**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

#### **V MONOGRAPHS IN PROGRESS**

**436 Diamorphine Tablets MC3(15)12**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

**437 Estradiol Vaginal Tablets MC3(15)13**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

**438 Fluticasone and Salmeterol Inhalation Powder, Pre-dispensed MC3(15)14**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

**439 Fluticasone and Salmeterol Pressurised Inhalation, Suspension MC3(15)15**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

**440 Olanzapine preparations MC3(15)16**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

**Olanzapine Tablets**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

**Olanzapine Orodispersible Tablets**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

441 **Soluble Prednisolone Tablets** MC3(15)17

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

442 **Vecuronium Bromide Injection preparations** MC3(15)18

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

VI **REVISIONS**

443 **Levonorgestrel Tablets** MC3(15)19

Data had been received from one MAH following a request to increase limits for content and related substances.

**Content** The MAH had previously requested the content limits be increased to 93.0 to 105.0. Data had now been received in support of this change. Members agreed that the data did not support the change and the current limits of 95.0 to 105.0% should be retained.

**Identification** The MAH had provided a HPTLC method to replace the stand alone LC procedure in the draft monograph. Members agreed that the HPTLC method should be included in the draft monograph as it would be more efficient for the analyst.

**Dissolution** Bayer proposed a new method to control the dissolution requirement. Upon review members agreed it was not suitable for compendia purposes as it utilised technology that was not commonly used.

Solution (1) should be prepared by dilution in dissolution medium.

The Secretariat agreed to investigate more stringent system suitability criteria for the LC system.

Members discussed the option of increasing the dissolution volume to 900 mL as the MAH had argued that this was better than the 500 mL in the draft monograph. Members agreed that this did give a more definitive end point, however, questioned if the use of 500 mL was a more discriminatory test. The Secretariat noted that this was a low dose tablet and the sample may be too dilute to achieve a suitable response. Members agreed that the method should be retained but further investigation should be performed regarding the optimum wavelength to use (potentially 240 nm) to ascertain if a 900 mL volume could be used. As this procedure had been harmonised with the International Pharmacopoeia, the Secretariat would discuss any potential changes with them.

**Related substances** Members agreed that the run time indicated under (g) in chromatographic conditions should apply to solution (1) only.

The Secretariat agreed to investigate more stringent system suitability criteria for the LC system.

**Assay/UofC** The MAH had requested that a second procedure was published along with an instruction to the analyst that only one method was required to be performed. The Secretariat informed members that this was not usual BP practice and, given that the alternative method was not considered superior to the current method, should not be included in the monograph.

Members agreed that solution (1) should be amended to take into account displacement volume due to the tablet matrix.

- 444 Lorazepam Preparations MC3(15)20**
- The Secretariat informed members that the monographs for these products were considered in need of updating/strengthening. The draft monograph had been prepared in-line with the European Pharmacopoeia parent monograph and other available information. Members agreed that the Laboratory should be asked to investigate the methods in the drafts for Lorazepam Tablets and Lorazepam Tablets.
- 445 Phenobarbital Preparations MC3(15)21**
- The Secretariat informed members that the monographs for these products were considered in need of updating/strengthening. These monographs were not the highest priority for the Laboratory to be working on, however, the Secretariat has been working with academic faculties who were willing to investigate these. Members agreed that the draft monographs should be investigated for Phenobarbital Elixir, Phenobarbital Injection and Phenobarbital Tablets. Members further noted that there were no MAH for Phenobarbital Sodium Tablets and recommended that the monograph was omitted.
- 446 Prednisolone Sodium Phosphate Oral Solution MC3(15)22**
- Related substances** A more dilute product was now available and the Secretariat had amended the preparation of solution (1) in the draft monograph to reflect this.
- Assay** The MAH indicated that parabens interfered with the principal peak in the chromatography. Members recommended that a more suitable method should be investigated. The Secretariat agreed to contact stakeholders to ask for their in-house procedures for review. It was further noted that Prednisolone Enema products contained parabens and therefore the Assay method in the Prednisolone Enema monograph may provide a useful basis for an improved test.
- 447 Vinblastine Injection MC3(15)23**
- There were two MAH for this product.
- Labelling** Members agreed that the amended statement in the draft monograph should be published.
- Members also noted that there were strict labelling and packaging requirements for pharmaceuticals and questioned the purpose of labelling statements in individual monographs. The Secretariat agreed to discuss the concerns of the group with EAG PCY at their next meeting.
- 448 Vincristine Injection MC3(15)24**
- There were three MAH for this product. Members agreed to send the Secretariat comments on the draft monograph for consideration.
- The monograph had been amended to reflect the marketed products (solutions for injection).
- Labelling** Members agreed that “weight of anhydrous vincristine sulfate contained in it” should be deleted.
- Members noted that there were strict labelling and packaging requirements for pharmaceuticals and questioned the purpose of labelling statements in individual monographs. The Secretariat agreed to discuss the concerns of the group with EAG PCY at their next meeting.

**VII EUROPEAN PHARMACOPOEIA COMMISSION**

Members were directed to log-in to the BP website to view the latest text from the Ph. Eur.

**VIII ANY OTHER BUSINESS**

No further items were raised for discussion.

**Date of Next Meeting**

Wednesday 22<sup>nd</sup> September 2015.