BRITISH PHARMACOPOEIA COMMISSION

EXPERT ADVISORY GROUP: MEDICINAL CHEMICALS 3

SUMMARY MINUTES

A meeting of Expert Advisory Group (EAG): Medicinal Chemicals 3 (MC3) was held at 151 Buckingham Palace Road, London SW1W 9SZ on Wednesday 28th September 2016.

Present: Mr V Fenton-May (*Chairman*), Professor E Williamson (*Vice Chair*), Professor M Almond, Mr M Tubby, Mr J Beach, Dr R Torano, Dr B Rackstraw, Mr I Williams.

In attendance: Mr A Evans, Ms S Gomersal, Dr G Kemp, Ms F Lee, Ms C Galdino, Ms M Nanasi.

Apologies: Dr K Pugh, Mr P Hampshire, Mr C Goddard, Dr J Beaman.

Introductory remarks

The Chairman welcomed everyone to the meeting.

Declaration of interests

Mr Torano declared interests in one or more agenda items and appropriate action was taken.

Emergency evacuation procedure **MC3(16)31**

The emergency evacuation procedure for Buckingham Palace Road was noted.

I MINUTES

The minutes and summary minutes of the meeting held on 25th February 2016 were confirmed.

II MATTERS ARISING FROM THE MINUTES

The following matters arising from the meeting held on 25th February 2016 were noted.

The following new monographs were published in the BP 2017:
Ferrous Fumarate and Folic Acid Capsules
Gabapentin Tablets, Capsules and Oral Solution
Co-cyprindiol Tablets

Acarbose Tablets

The draft monograph had been amended and the lab investigation begun. However due to issues with the system suitability in the related substances and assay procedures, the analysis had been delayed. The Secretariat had contacted the MAH for advice and further information. It was anticipated that the Laboratory could continue this work once further information had been received. Members noted that this procedure was undergoing informal harmonisation with other pharmacopoeias.

Colecalciferol Tablets

The final statement regarding the prescribing of “calciferol” had been deleted as it was considered obsolete. The review regarding identification was ongoing.

Dutasteride Capsules

Revision of the monograph was in progress and the Secretariat were awaiting further information from the manufacturer.

Dydrogesterone Tablets

The previously omitted monograph had been re-introduced to the BP as the product was available in some countries where the BP had legal effect.

Dihydrocodeine Preparations

The Laboratory requisition had been submitted and the walkthrough completed. Work was due to begin shortly.

Lorazepam Preparations

The Laboratory requisition had been submitted and the walkthrough was to be conducted prior to the commencement of the investigation.

Clobazam Oral Suspension

Identification A The Laboratory had investigated the mobile phase and confirmed that the correct mobile phase was 40 volumes acetone and 60 volumes hexane, this would be included in the BP 2018.

III MONOGRAPHS

496 SILDENAFIL PREPARATIONS MC3(16)32

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

497 PRAMIPEXOLE PREPARATIONS MC3(16)33

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

498 MORPHINE PREPARATIONS MC3(16)34

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

499 METHADONE PREPARATIONS MC3(16)35

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

500 OLANZAPINE PREPARATIONS MC3(16)36

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

501 HYOSCINE BUTYLBROMIDE PREPARATIONS MC3(16)37

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

502 ERGOCALCIFEROL TABLETS MC3(16)38

The Ergocalciferol Tablets monograph had been updated with the agreed changes from the meeting held in February 2016.

The withdrawn EPCRS has been replaced with 'cholecalciferol for system suitability EPCRS', which contained the required impurities.

Assay: As the current published monograph used hazardous reagents, the Secretariat proposed a new procedure in the draft monograph. The draft method was based on the uniformity of content procedure and was accepted by the EAG.

503 PYRIDOXINE TABLETS MC3(16)39

A member from the Licensing Division requested a revision to the Pyridoxine Tablets monograph. The draft monograph had been revised based on new methods from the Ph. Eur. API monograph as the published BP monograph contained a TLC Related substances test and a UV Assay method.

504 SOLUBLE PREDNISOLONE TABLETS MC3(16)40

A query from a user stated that the current Dissolution HPLC method was unsuitable since prednisolone sodium phosphate eluted on the solvent front. The interference from the solvent caused a significant error and the method needed to be amended. The monograph was revised using the same HPLC conditions as the Assay. In addition, one of the solutions of the Assay test was amended to a more appropriate concentration.

Dissolution the LC conditions were adapted from the Assay procedure, members agreed the revision should be included in the monograph.

Assay Solution (1), the concentration of the solution was amended to ensure the correct peak area response would be achieved.

505 NORETHISTERONE & ETHINYLESTRADIOL TABLETS MC3(16)41
(GESTODENE & ETHINYLESTRADIOL TABLETS)

A draft new monograph for Norethisterone and Ethinylestradiol Tablets was presented to the EAG, based on the Gestodene and Ethinylestradiol Tablets monograph.

The Secretariat proposed simultaneous Laboratory investigation of the Norethisterone and Ethinylestradiol Tablets.

Identification, Dissolution, Related substances, Uniformity of Content and Assay were all replicated from the Gestodene and Ethinylestradiol Tablets monograph, with appropriate sample concentrations to suit the available strength of tablets. The Laboratory agreed to fully investigate the methods.

506 VINBLASTINE INJECTION MC3(16)42

Definition The draft monograph had been split into two sections, both with analytical procedures intended to control the two available pharmaceutical forms.

Members agreed that the revised monograph should be published in the BP 2018.

507 ALPROSTADIL PREPARATIONS MC3(16)43

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

ALPROSTADIL CREAM

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

ALPROSTIDIL URETHRAL STICKS

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

508 CLOMIFENE TABLETS MC3(16)44

As part of the revision programme to update monographs using out dated methodology, the monograph had been amended to include an HPLC related substance test and Assay.

Content the limits 95.0-105.0% were accepted, subject to comments from Stakeholders.

Identification members recommended including an IR test as it would be a stand alone procedure that would negate the need for identification test B which used pyridine.

Related substances and Assay the LC procedure was adapted from the Ph Eur monograph Clomifene Citrate.

Z-Isomer members suggested revising this test to remove the use of chloroform.

509 CYTARABINE INJECTION MC3(16)45

As part of the general review and update of monographs, Cytarabine Injection was identified for review as it required a more selective Related substances procedure.

Related substances the TLC procedure was replaced by the HPLC method used in the Assay. The Laboratory would need to fully investigate the methods for suitability.

510 MIDAZOLAM OROMUCOSAL SOLUTION MC3(16)46

The Secretariat informed members that they had attended a meeting with Licensing and a new manufacturer of midazolam oral solution. The MAH was having difficulty in meeting the requirements in the current BP monograph and wanted an opportunity to meet to discuss this. The manufacturer will be providing further data to justify a change to the Related substances limits and content requirements.

511 NALOXONE INJECTION MC3(16)47

The monograph was identified as requiring updating following an editorial change to the monograph to remove the dispensing and supply statements.

Related substances the Ph. Eur. HPLC method had been adapted and included in the draft monograph. Members recommended that the wording of solution (1) was amended in line with the usual BP editorial style.

Bacterial Endotoxins members agreed to remove the test as it was covered by the general monograph.

512 NANDROLONE DECANOATE INJECTION MC3(16)48

The monograph for Nandrolone Injection recently underwent a minor revision and it was noted at the time that methods in the monograph required updating. The Secretariat had included an HPLC Assay and Related substances test, both based upon the methods from the Ph. Eur. API monograph.

Content members recommended that the limits were specified as 95.0-105%, subject to comments from MAH.

Related substances the Ph Eur method was adapted and included in the draft monograph. Limits were in line with ICH and the MAH limits.

Assay Members agreed with the revision but noted that the retention time of the principal peak should be included. Members agreed that the methods could be published in the BP 2018, subject to comments from MAH.

514 PHYTOMENADIONE PREPARATIONS MC3(16)49

The Secretariat was contacted by a user regarding Identification test B in the Phytomenadione Injection monograph; they questioned the suitability of the UV test in the BP monograph, the wavelengths of the maxima/minima being reported as inconsistent. The user indicated that a peak comparison in the Assay between solutions (1) and (2) would be more appropriate. The Secretariat reviewed the monograph and has updated the methods where required.

Identification test B was updated to an HPLC peak comparison in the Assay.

Related substances the test from the parent Ph. Eur. monograph was included. The MAH identifies additional impurities to the Ph. Eur. API monograph. Members suggested contacting the MAH to find out more information about the impurities and

whether they can justify the wide content limits (90-115%) currently in the monograph.

515 ROTIGOTINE TRANSDERMAL PATCHES MC3(16)50

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

IV FOR INFORMATION

Members Details MC3(16)51

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

MC3 Work Programme MC3(16)52

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

V EUROPEAN PHARMACOPOEIA MC3(16)53

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

VI ANY OTHER BUSINESS MC3(16)54

No further items were raised for discussion.

VII NEXT MEETING MC3(16)55

Tuesday 21 February 2017