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 27th September 2017.

Present: Mr V Fenton-May (*Chairman*), Professor M Almond (*Vice Chair*), Dr J Beaman, Mr C Goddard, Dr R Torano, Dr B Rackstraw, Mr I Williams.

In attendance: Mr A Evans, Dr G Kemp, Ms M Wall, Ms F Lee, Ms D Ballottin.

Apologies: Dr K Pugh, Mr M Tubby, Mr P Hampshire, Ms C Galdino.

Introductory remarks

The Chairman welcomed everyone to the meeting including Ms Lee and Ms Ballottin from the British Pharmacopoeia Laboratory.

The Chairman noted that this was his last meeting following announcement of his retirement from the group. Members thanked the Chairman for his long and dedicated service to the group.

Declaration of interests

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

Emergency evacuation procedure **MC3(17)19**

The emergency evacuation procedure for Buckingham Palace Road was noted.

I MINUTES **MC3(17)20**

The minutes and summary minutes of the meeting held on 21st February 2017 were confirmed subject to the correction of a minor typographical error.

II MATTERS ARISING FROM THE MINUTES

The following matters arising from the meeting held on 21st February 2017 were noted.

Acarbose Tablets

The monograph was held back from publication after the marketing authorisation holder indicated that there was a problem with their current Related substances method. The company had agreed to supply the BP with the new validated procedure.

Colecalciferol Tablets

The review of identification was ongoing.

Rotigotine Transdermal Patches

It was noted that the monograph would only be published once the Ph Eur had published the monograph for the API.

Fluorescein Preparations

A new related substances test was under investigation.

It was noted that the Secretariat were awaiting data from various MAH prior to progressing the following monographs:

- Midazolam Oromucosal Solution
- Dutasteride Capsules
- Phytomenadione Preparations
- Acarbose Tablets

III MONOGRAPHS FOR THE BP 2019

526 LORAZEPAM PREPARATIONS MC3(17)21
LORAZEPAM TABLETS
LORAZEPAM INJECTION

The BP Laboratory had completed their investigations and the draft monographs had been revised accordingly.

Content The content limits were amended to 92.5-105.0%.

Identification The current Related substances method (TLC) was verified by the BP Laboratory for use as an identification test. It was agreed that a peak comparison in the Assay would be included as a second identification.

Related substances The Laboratory had confirmed the suitability of the draft method, with minor modifications and agreed limits for impurity E.

Uniformity of content The BP Laboratory had confirmed the suitability of the method in the draft monograph. This was an isocratic HPLC method based on the Ph. Eur. API Related substances test.

Assay The method in the draft monograph was confirmed by the BP Laboratory with the modification of using whole tablets instead of powdered tablets.

Impurities Members recommended adding an impurities section in the monograph to indicate the impurities controlled are the same as those in the Ph. Eur.

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

527 TOLTERODINE PREPARATIONS MC3(17)22
TOLTERODINE TABLETS
TOLTERODINE PROLONGED-RELEASE CAPSULES

The draft monographs would be published in a future edition of the BP.

528 QUETIAPINE PREPARATIONS MC3(17)23
QUETIAPINE TABLETS
QUETIAPINE PROLONGED-RELEASE TABLETS

The draft monographs would be published in a future edition of the BP.

529 DIHYDROCODEINE PREPARATIONS MC3(17)24
DIHYDROCODEINE TABLETS
DIHYDROCODEINE PROLONGED-RELEASE TABLETS
DIHYDROCODEINE INJECTION
DIHYDROCODEINE ORAL SOLUTION

Following an investigation by the BP Laboratory, draft monographs for Dihydrocodeine Preparations were presented and agreed by members at the February 2017 EAG meeting. The draft monographs were posted for public consultation and no comments were received.

Members recommended adding a statement to protect the samples from light.

Related substances (Injection only) Members recommended changing “impurity A” references to “codeine”.

Related substances (Oral Solution only) Members recommended removal of statement (g) under chromatographic conditions since the method was gradient-based.

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

530 VARDENAFIL PREPARATIONS MC3(17)25
VARDENAFIL TABLETS
ORODISPERSIBLE VARDENAFIL TABLETS

The draft monographs would be published in a future edition of the BP.

531 FLUTICASONE AND SALMETEROL PRESSURISED INHALATION, SUSPENSION MC3(17)26

The Fluticasone and Salmeterol Pressurised Inhalation, Suspension monograph was first published in the BP 2016 based on a data received from MAH.

The content limits were amended in consultation with EAG PCY. Furthermore, additional impurity retention times were also included in the Related substances test in order to aid identification of impurity peaks observed in the sample solution chromatography.

Content The limits were amended to 75.0-101.0% of stated amount for Fluticasone and 71.5-96.5% of the stated amount for Salmeterol (± 15% of ex-actuator value), following consultation with manufacturers, EAG PCY and reviewing EMA guidance.

Related substances Additional relative retention times were given for impurities.

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

532 DIFLUCORTOLONE PREPARATIONS MC3(17)27
DIFLUCORTOLONE CREAM
DIFLUCORTOLONE OILY CREAM
DIFLUCORTOLONE OINTMENT

The Secretariat had amended the methods to remove the need for the external standard in the draft monographs. The Assay was not updated so did not contain a system suitability requirement and therefore would require the Laboratory investigating a suitable recommendation when the diflucortolone valerate BPCRS was under retest. The Secretariat had proposed contacting the MAH to see if there are updated methods that could be used to update the monographs.

Content Members questioned whether the limits should be reduce to 95.0 to 105.0%.

Storage Members proposed including storage conditions.

Members also questioned the reasoning behind 2 separate monographs for Diflucortolone Cream and Diflucortolone Oily Cream. The Secretariat agreed to follow up with the BNF.

It was agreed that the Secretariat would contact the MAH for updated methods. The draft monographs would be included in a future BP publication.

533 PROGESTERONE INJECTION MC3(17)27

Following the withdrawal of Progesterone Impurity C EPCRS, the system suitability solution had been updated to Progesterone for system suitability EPCRS (containing impurity C). However, it was found that the concentration was too low to detect impurity C and therefore determine the resolution requirement.

Related substances The concentration of solution (3) was amended to 0.04% (from 0.004%), allowing detection of impurity C.

Assay The same changes as the Related substances were.

Impurities Members highlighted that an Impurity statement needed to be added to the monograph.

The draft monograph would be published in a future edition of the BP.

534 NALOXONE INJECTION MC3(17)29

Following the last update of the monograph in the BP 2018, one MAH provided comments after the public consultation window had closed. The Secretariat had produced a draft revised monograph that incorporated the comments received.

Related substances The column packing was updated for the chromatographic

conditions.

Labelling The second statement was corrected.

Members agreed to the amendments in the draft monograph and highlighted editorial amendments required. The draft monograph would be published in a future edition of the BP.

IV MONOGRAPHS FOR BP2019+

535 METHADONE PREPARATIONS MC3(17)30

METHADONE TABLETS
METHADONE INJECTION
METHADONE ORAL SOLUTION
METHADONE ORAL CONCENTRATE
METHADONE HYDROCHLORIDE

The draft monographs were agreed for publication at the September 2016 meeting, however the Secretariat decided to not publish them on the grounds that they were untested for some difficult to analyse pharmaceutical forms.

The BP Laboratory agreed to investigate the methods in the draft monographs prior to publication.

536 MOMETASONE PREPARATIONS MC3(17)31

MOMETASONE POWDER FOR INHALATION

The draft monograph for Mometasone Powder for Inhalation would be published in a future edition of the BP.

MOMETASONE AQUESOUS NASAL SPRAY
MOMETASONE CREAM
MOMETASONE OINTMENT
MOMETASONE SCALP APPLICATION

The Mometasone Preparations monographs contained either no Related substances test or TLC tests and therefore subject to revision.

Content limits of 95-105% were included for all preparations. MAH would be invited to provide stability data if any widening of the limits were required.

Identification a modified TLC procedure had been drafted for all preparations.

Related substances the method had been adapted from the Ph. Eur. API procedure. Limits were based on UK licensed products and ICH guidelines.

Assay the drafted method was adapted from the Ph. Eur. API HPLC procedure.

537 BETAMETHASONE AND NEOMYCIN PREPARATIONS MC3(17)32

BETAMETHASONE AND NEOMYCIN EYE DROPS
BETAMETHASONE AND NEOMYCIN EAR DROPS

BETAMETHASONE AND NEOMYCIN NOSE DROPS

The draft monographs would be published in a future edition of the BP.

538 INOSITOL NICOTINATE API AND TABLETS MC3(17)33

The API and Tablets monograph contained a TLC Related substances test. The Secretariat had revised the methods based on the Ph. Eur. myo-Inositol monograph as an acceptable procedure for the control of impurities.

The BP Laboratory will investigate draft method prior to publication.

539 SPIRONOLACTONE TABLETS MC3(17)34

The monograph was amended as it contained chloroform in the related substances test and a non-specific assay. The Secretariat had drafted a monograph based on Spironolactone Oral Solution.

The Secretariat will post the draft monograph for public consultation.

540 TAMOXIFEN PREPARATIONS MC3(17)35
TAMOXIFEN TABLETS

The Secretariat had produced a draft monograph. The Secretariat will send the draft monograph to MAH.

TAMOXIFEN ORAL SOLUTION

The draft monograph would be published in a future edition of the BP.

IV FOR INFORMATION

Members Details MC3(17)36

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

MC3 Work Programme MC3(17)37

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(17)38

Members were directed to go to the BP website to view the latest text from the Ph. Eur.

VI ANY OTHER BUSINESS

No further items were raised for discussion.

VII NEXT MEETING

TBC.