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 10 South Colonnade, Canary Wharf, London E14 4PU on Monday 8th October 2018.

Present: Professor M Almond (*Chairman*), Mr J Beach, Mr C Goddard, Dr R Torano, Mr I Williams.

In attendance: Mr A Evans, Ms M-L Wall, Mr M Whaley (PM only), Ms K Busuttil, Ms M Nanasi.

Apologies: Dr J Beaman, Mr P Hampshire, Dr K Pugh, Dr B Rackstraw.

Introductory remarks

The Chairman welcomed everyone to the meeting.

The Chairman noted that this was his first meeting as Chair and invited all to participate fully in the discussions.

Declaration of interests

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

Emergency evacuation procedure

The emergency evacuation procedure for 10 South Colonnade was noted.

I MINUTES MC3(18)1

The minutes and summary minutes of the meeting held on 27th September 2017 were confirmed.

II MATTERS ARISING FROM THE MINUTES MC3(18)2

The following matters arising from the meeting held on 27th September 2017 were noted.

Acarbose Tablets MC3(18)3

The marketing authorisation holder had sent the updated data package to the Secretariat in early October. The updated draft monograph would be discussed at the next EAG meeting after the Secretariat had time to review the information.

Midazolam Oromucosal Solution MC3(18)4
Phytomenadione Preparations

Awaiting stability data from MAH prior to revising limits.

Diflucortolone Preparations MC3(18)5

The monographs will be amended to remove the use of BPCRS in the BP 2020

Progesterone Injection **MC3(18)6**

The Secretariat confirmed that the EPCRS could be used in the injection monograph to replace the BPCRS and agreed this would be published in the BP 2020.

The Secretariat were awaiting data from various MAH prior to progressing the following monographs: **MC3(18)7**

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

Betamethasone and neomycin eye drops **MC3(18)8**
Betamethasone and neomycin ear drops
Betamethasone and neomycin nose drops

The Secretariat confirmed that the Content requirement for neomycin would be in terms of the combined neomycin isomers, with isomer C limited to 15% of the total neomycin content.

Laboratory investigations were in progress for: **MC3(18)9**

- Methadone preparations
- Tamoxifen preparations
- Mometasone preparations

Future Laboratory investigations will be scheduled for: **MC3(18)10**

- Alprostadil preparations
- Norethisterone & ethinylestradiol tablets
- Norgestimate & ethinylestradiol tablets
- Gestodene & ethinylestradiol tablets
- Clomifene Tablets
- Cytarabine Injection
- Pyridoxine Tablets

Fluorescein Preparations **MC3(18)11**

A new test for Related substances was being investigated.

BP 2019 **MC3(18)12**

9 new monographs and 7 significantly revised monographs that were the responsibility of EAG MC3 had been published in the BP 2019. Members were thanked for their contributions and hard work, helping to publish this number of monographs.

III MONOGRAPHS FOR THE BP 2020

541 AMITRIPTYLINE ORAL SOLUTION MC3(18)13

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

AMITRIPTYLINE TABLETS

The Laboratory had completed its investigation into the methods and made recommendations as necessary. The Secretariat had updated the draft monographs.

Dissolution (Tablets) The limits would be amended prior to publication, if necessary, to reflect the outcome of the BP Dissolution policy review.

Related substances The draft method would be updated to reflect the names of the impurities where relevant and their retention times.

Members agreed that the monograph should be published on the website at the next public consultation and be published in the BP 2020 subject to comments from manufacturers.

542 CAPECITABINE TABLETS MC3(18)14

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

543 SODIUM PICOSULFATE ORAL DROPS MC3(18)15

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

544 CABERGOLINE TABLETS MC3(18)16

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

545 CALCIPOTRIOL AND BETAMETHASONE PREPARATIONS MC3(18)17

- CALCIPOTRIOL AND BETAMETHASONE GEL
- CALCIPOTRIOL AND BETAMETHASONE OINTMENT
- CALCIPOTRIOL AND BETAMETHASONE CUTANEOUS FOAM

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

546 ROTIGOTINE TRANSDERMAL PATCHES MC3(18)18

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

547 SILDENAFIL PREPARATIONS MC3(18)19

- Sildenafil Tablets
- Sildenafil Chewable Tablets
- Sildenafil Orodispersible Tablets
- Sildenafil Orodispersible Films
- Sildenafil Injection
- Sildenafil Oral Suspension

Related substances – impurity setting Limits in the draft monographs were discussed and, although there was basic agreement, there were some fundamental concerns regarding limit setting in pharmacopoeias. Members informed the Secretariat that there were often costs associated (usually for the API monographs) when the products were global, and the APIs needed to be licensed (outside of the EU). This process was often costly and, where the products were investigated using ICH Q9 principles, in conflict with ICH requirements. The Secretariat informed members that there was a specific BP project being undertaken in this area and would put their concerns to this group.

The Secretariat agreed to investigate if the identification of impurities A and D were still required in the method, or if the impurities could now be controlled as unspecified impurities.

548 LEVONORGESTREL TABLETS MC3(18)20

Identification A The Members agreed that the preparation of solution (1) in the draft monograph should be to a larger volume to remove errors in diluting to 2mL. Members also agreed that the visualisation should be under UV (366 nm) light only and there was no need to spray the plate.

Dissolution Members requested that the Secretariat check the concentrations of the Dissolution procedure were correct in the draft monograph.

549 VECURONIUM BROMIDE FOR INJECTION MC3(18)21

The related substances method for the injection was based on the Ph Eur API monograph. Following minor amendments published to the API monograph, the Secretariat had written a revised monograph for publication in the BP 2020.

Related substances Members agreed that the limit for impurity C should be retained at 1% and that the disregard solution concentration and limit should be 0.1% (as ICH). The Secretariat agreed to investigate the column in the draft monograph was the same as that specified in the Ph. Eur. Knowledge database.

Content Members asked the Secretariat to ensure that the lower (93%) content limit was supported with data from the MAH.

550 CLOBAZAM ORAL SUSPENSION MC3(18)22

Dissolution Members agreed that the method should be included in the BP and that the Q=80% in 20 minutes was acceptable for this product as the non-dissolved particles were already dispersed in the suspension.

Related substances Given the dissolution required to be performed protected from light, members requested that the requirement was included in the assay and related substances test.

551 ZUCLOPENTHIXOL HYDROCHLORIDE & PREPARATION MC3(18)23

- Zuclopenthixol Hydrochloride (API)
- Zuclopenthixol Tablets

Related substances (API and Tablets) Members noted that the procedure should be carried out protected from light and that the composition of mobile phase C confirmed.
Identification (Tablets) Members agreed that the two methods in the revised monograph would be sufficient to control the identification requirements.

Dissolution the method in the revised monograph was in line with the MAH method and members agreed it should be retained.

Assay the method in the revised monograph was in line with the MAH method and members agreed it should be retained.

552 TRIAMCINOLONE PREPARATIONS MC3(18)24

- TRIAMCINOLONE ACETONIDE INJECTION
- TRIAMCINOLONE NASAL SPRAY
- TRIAMCINOLONE OROMUCOSAL PASTE
- TRIAMCINOLONE OINTMENT
- TRIAMCINOLONE CREAM

Triamcinolone Oromucosal Paste Members requested that the Secretariat investigate if there is still a requirement for this monograph as the product appeared to not be available.

Definition (Acetonide Injection) The Secretariat agreed to review the statement as it contained phrases that were not common in the BP.

Related substances The Secretariat agreed to include a linear gradient step in the gradient table, to return the mobile phase to the original conditions.

Uniformity of content Members recommended that a test for uniformity of content would be required if any of the products were available in single dose containers.

IV MONOGRAPHS FOR THE BP 2021+

553 DUTASTERIDE CAPSULES MC3(18)25

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

554 ALENDRONIC ACID AND COLECALCIFEROL TABLETS MC3(18)26

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

V FOR INFORMATION

555 PHENOBARBITAL INJECTION MC3(18)27

The Secretariat thanked members for their help and swift responses to an emergency regarding the supply of this material to hospitals. The swift actions and way forward for this monograph led to the product being release being expedited. The draft monograph was now available on the BP website.

556 TAMPER PROOF FORMULATIONS MC3(18)28

Products, such as oxycodone tablets, were known to be abused parenterally. Companies have been investigating formulations that make this type of abuse of the product very difficult. By creating a formulation that forms a gel when ground in solvents, making it impossible to inject, however, these products also form a gel when using the BP sample preparations for analytical testing. The Secretariat had been in contact with an MAH with this issue to amend a monograph to control their product, however, there was concern that this would instruct an addict in how to abuse the medicine. Members indicated a statement could be included indicating the specific methods in the monograph may not be suitable for formulations that were designed to

reduce the potential for abuse by injection, however, the limits in the monograph would still apply.

Members Details **MC3(18)29**

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

MC3 Work Programme **MC3(18)30**

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.

VI EUROPEAN PHARMACOPOEIA MC3(18)31

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

VII ANY OTHER BUSINESS

No further items were raised for discussion.

VIII NEXT MEETING

26th February 2019.