BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group MC1: Medicinal Chemicals

SUMMARY MINUTES

A meeting of Expert Advisory Group (EAG): Medicinal Chemicals 1 (MC1) was held at 10 South Colonnade, Canary Wharf, London, E14 4PU on Tuesday 25 June 2019.

Present: Professor A G Davidson *(Chair),* Professor Donald Cairns *(Vice-Chair),* Dr Hannah Batchelor, Dr J C Berridge, Dr E Bush, Mr A J Caws, Mr D Deutsch, Dr E Gray, Dr J Lough and Mr D Malpas, Mr S Nolan.

In attendance: Ms H Corns, Mr L Elanganathan, Mr H Makwana, Ms K Busuttil, Ms M Nanasi and Ms L Piare.

Apologies: Dr S Bale, Mr P Fleming

INTRODUCTORY REMARKS

555 **Welcome** The Chair welcomed members to the meeting and introduced Dr H Batchelor and Mr S Nolan as new experts for the Expert Advisory Group on Medicines Chemicals 1 (EAG MC1). The chair also welcomed Ms M Nanasi, Ms K Busuttil and Ms L Piare from the BP Laboratory

Confidentiality Members were reminded that all papers and minutes were confidential and should not be disclosed outside the BP Commission.

Declaration of Interests Professor D Cairns, Mr A Caws and Dr E Bush declared interests in one or more agenda items and appropriate action was taken.

556 Emergency evacuation procedure

The emergency evacuation procedure for 10 South Colonnade was noted.

557 BP Update

Members were provided with an update on BP staff changes, the launch of the recent consultation on Analytical Quality by Design (deadline for comments 31 August 2019) (https://www.gov.uk/government/consultations/consultation-on-the-application-of-analytical-quality-by-design-aqbd-principles-to-pharmacopoeial-standards-for-medicines) and the introduction of a 'How to use the BP' guide available on the BP website (https://www.pharmacopoeia.com/how-to-use-the-bp).

558 MINUTES

The minutes and summary minutes of the meeting held on 5 December 2018 were confirmed.

559 Matters Arising

Matters arising from the 5 December 2018 meeting were noted.

MONOGRAPHS

560 Bendroflumethiazide Tablets (revision)

Content A tighter content requirement of 95.0 to 105.0% was accepted and justified by the data provided, subject to stakeholder comments.

Identification A A TLC identification method had been drafted and would be evaluated by the BP Laboratory.

Dissolution A dissolution test had been drafted and would undergo laboratory evaluation. Members accepted the proposed Q limits of 75% in 45 minutes subject to stakeholder comments

Related Substances An LC method has been drafted and the suitability would be confirmed by laboratory evaluation. The draft limits proposed are:

- Impurity A peak: 1.0%, as per current BP monograph – the laboratory investigations will consider if a lower limit as per the specifications can be used.
- Secondary peak: 0.5%, as per identification threshold
- Sum of secondary peak: 1.5%
- Disregard peak: 0.1%, as per reporting threshold

Assay An isocratic LC method has been drafted and the suitability would be confirmed by laboratory evaluation.

561 Repaglinide Tablets (new)

The draft monograph for Repaglinide Tablets would be included in a future BP publication, subject to amendments and comments from manufacturers.

562 Paracetamol preparations: (revision)
Paracetamol & Caffeine Tablets (revision)
Paracetamol & Caffeine Soluble Tablets (revision)
Co-codamol Tablets (revision)
Co-codamol Effervescent Tablets (revision)
Co-codamol Capsules (revision)
Co-dydramol Tablets (revision)
Paracetamol, Codeine Phosphate & Caffeine Tablets (revision)
Paracetamol, Codeine Phosphate & Caffeine Capsules (revision)

The Secretariat informed members that following the drafting of methods to revise Paracetamol combination products, laboratory evaluation had been scheduled.

Dissolution (Co-codamol Tablets, Co-codamol Capsules, and Co-dydramol Tablets) Members accepted the proposed Q limits of 75% in 45 minutes subject to stakeholder comments.

Related substances (Co-codamol Tablets, Co-codamol Effervescent Tablets, Co-codamol Capsules, Co-dydramol Tablets, and Paracetamol, Codeine Phosphate and Caffeine Tablets, and Paracetamol, Codeine Phosphate and Caffeine Capsules) The Secretariat presented a review of the registered specifications for 4-chloroacetanilide (impurity K) and 4-aminophenol (impurity J). The Secretariat agreed to

consider the laboratory results to propose suitable limits for these impurities at a future meeting.

563 Busulfan preparations:
Busulfan Tablets (revision)
Busulfan Sterile Concentrate (new)

Busulfan Tablets It was decided that the work on this monograph would be paused and restarted in tandem with the next BPCRS re-test.

Busulfan Sterile Concentrate The Secretariat had updated the draft monograph following comments received from members during the December 2018 meeting and manufacturer comments. The draft monograph for Busulfan Sterile Concentrate would be included in a future BP publication, subject to comments from manufacturers.

564 Propofol Injection (revision)

Lysolecithin The lab reported that the draft revised method was suitable for controlling lysolecithin from egg sources in Propofol Injection; however, it would not be suitable for lysolecithin from soya sources. Members agreed that the revised test was acceptable for publication, with a direction to apply the test to Propofol Injection products containing egg lecithins and a limit for lysolecithins from soya specified under Production.

Assay It was noted that as propofol injection was an emulsion, a weight per mL determination may be more suitable for assay as the product was viscous. It was agreed that a change to weight per mL determination would be included in the draft monograph subject to stakeholder comments.

565 Nevirapine preparations:
Nevirapine Tablets (new)
Nevirapine Prolonged-release Tablets (new)

The draft monographs for Nevirapine Tablets and Nevirapine Prolonged-release Tablets would be included in a future BP publication, subject to amendments and comments from manufacturers.

566 Itraconazole Capsules (revision)

Dissolution Following publication of Itraconazole Capsules in the BP 2019, 2 manufacturers had reported challenges meeting the dissolution criteria in the new monograph. Extending the procedure time or reducing the limit were proposed as resolutions, and the Secretariat agreed to confirm what would be acceptable to the Licensing Division.

567 Cisplatin Injection (revision)

Members agreed that the limit for trichloroammineplatinate should be changed in the BP monograph for Cisplatin Injection from 1.5% to 3.0%.

568 Amantadine preparations:
Amantadine Capsules (revision)

Amantadine Oral Solution (revision)

Draft revised monographs for Amantadine preparations had been posted on the BP website for public consultation and minor changes made as the result of comments received.

Members noted discrepancies in the Dissolution and Related substances solutions which would be amended prior to publication of the draft revised monographs.

569 MC1 Work status and updates

The MC1 work programme was presented to members for information.

570 Pharmeuropa Update

Updates to Ph. Eur. monographs following the recent Pharmeuropa public consultation cycles were reviewed. Members were made aware of the changes to the monograph for Aciclovir in the Ph.Eur. and agreed that the subsequent changes could be made to the finished product monographs to remove the requirements for Impurity O and Impurity A following adoption of the revised Ph. Eur. limits.

571 AOB

No items were raised.

572 Date of next meeting

Tuesday 3 December 2019