BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group: Antibiotics

SUMMARY **MINUTES**

A meeting of Expert Advisory Group: Antibiotics was held via videoconference on Tuesday 31st March 2020.

Present: Dr R Horder *(Chair),* Dr G Cook (*Vice-chair*), Dr G Clarke, Mr E Flahive, Dr W Mann, Prof J Miller, Dr M Pires, and Mr I Williams.

Apologies: Mr G Blake, Mr V Jaitely, Mr J Sumal

In attendance: Mr S Maddocks, Dr H Bowden, Ms K Busuttil and Ms M Nanasi.

Mr Flahive declared an interest in one or more items and took part in the discussions.

471 **Introductory remarks**

Welcome
The Chair welcomed Ms Busuttil and Ms Nanasi from the BP Laboratory.

Membership
Members were asked to let the Secretariat know if any of their details had changed.

472 **General Matters** **ABS(20)01**

Declaration of Interests
Members were reminded to declare specific interests as they arose during the meeting and to inform the Secretariat of any changes to their interests throughout the year.

Freedom of Information
Members were reminded that any FOI queries that they receive from the media were to be referred to the Secretariat.

I **MINUTES** **ABS(20)02**

473 The minutes for the meeting held on 9th December 2019 were confirmed.

II **MATTERS ARISING FROM THE MINUTES** **ABS(20)03**

474 The following matters arising from the meeting held on 9th December 2019 were noted.

Marbofloxacin Preparations (minute 365.21 refers) The monographs would be included in a future publication of the BP.

Ceftiofur Hydrochloride Suspension for Injection (minute 365.18 refers) The monograph would be included in a future publication of the BP.

Oxytetracycline Preparations (minute 372 refers) A laboratory report was pending for the assessment of the Related substance and Assay procedures.

Ciprofloxacin Preparations (minute 399 refers) A laboratory report was pending for the development of an Identification procedure and for the assessment of the Related substance and Assay procedures.

Co-Amoxiclav Preparations (minute 400 refers) A laboratory report was pending for the assessment of the Related substance procedure.

Enrofloxacin Preparations (minute 401 refers) The monographs would be included in a future publication of the BP.

Rifampicin Preparations (minute 402 refers) A laboratory report was pending for the assessment of the Identification, Related substance and Assay procedures.

Amoxicillin Preparations (minute 409 refers) A laboratory report was pending for the assessment of the Related substance procedure.

Lymecycline Capsules (minute 417.2 refers) The Secretariat were awaiting finalisation of the Ph Eur parent monograph before further developing the Related substances procedure in this monograph.

Bacterial Endotoxins (minute 417.4 refers) The Secretariat were seeking clarification on the additional information required to remove pyrogens test from remaining Ph. Eur. parent monographs.

Amikacin Injection (minute 417.8 refers) The Secretariat were looking at options for the assessment of the PAD Related substances procedure with a contract laboratory. The Secretariat had contacted an expert in EDQM regarding the use of PAD to explore potential for training and knowledge transfer to the BP laboratory.

Caspofungin for Injection (minute 417.15 refers) The monograph would be included in a future publication of the BP.

Ciclosporin Preparations (minute 417.16 refers) The monographs were awaiting finalisation of the Ciclosporin API monograph before proceeding with laboratory work.

Rifampicin Combination Preparations (minute 417.17 refers) The monographs would be included in a future publication of the BP.

Vancomycin Preparations (minute 427 refers) A laboratory report was pending for the assessment of the Related substance and Vancomycin B procedures.

Chloramphenicol Preparations (minute 428 refers) A laboratory report was pending for the development of an Identification procedure and for the assessment of the Dissolution, Related substance and Assay procedures.

Colistin Tablets (minute 444 refers) The Secretariat were to revise the monograph and ensure its suitability to cover unlicensed medicines

Norfloxacin Tablets (minute 445 refers) The Secretariat were to revise the monograph and ensure its suitability to cover unlicensed medicines.

Streptomycin Injection (minute 446 refers) The Secretariat were to amend the monograph for Streptomycin Injection for inclusion in the BP(Vet) and to create a separate monograph for the powder for injection requirement which would be evaluated for its suitability to cover unlicensed medicines.

Florfenicol Preparations (minute 447 refers) The monographs would be included in a future publication of the BP.

Nystatin Preparations (minute 448 refers) The Secretariat were to amend the monographs as previously agreed and circulate to manufacturers and the USP for comments. The ointment monograph would be assessed for its suitability to cover unlicensed medicines.

Polymyxin and Bacitracin Ointment (minute 449 refers) The Secretariat were to amend the Ointment monographs as agreed and circulate to manufacturers for comment.

Teicoplanin Injection (minute 450 refers) The monograph would be included in a future publication of the BP.

Erythromycin Preparations (minute 463 refers) The monographs had been amended as agreed and made available for public consultation. Minor comments had been received. The monographs were to be published in the BP 2021.

Clindamycin Preparations (minute 464 refers) The monographs had been amended as agreed and made available for public consultation. Minor comments had been received. The monographs were to be published in the BP 2021.

Fusidic Acid/Sodium Fusidate preparations (minute 465 refers) The monographs had been amended as agreed and made available for public consultation. No comments were received. The monographs were to be published in the BP 2021.

III MONOGRAPHS FOR THE BP 2022

475 Rifaximin Tablets (New) **ABS(20)04**

The monograph for Rifaximin Tablets would be published in a future edition of the pharmacopoeia.

476 Cefalexin Preparations **ABS(20)05**
Cefalexin Capsules (Revision)
Cefalexin Oral Suspension (Revision)
Cefalexin Tablets (Revision)

Draft revised monographs for Cefalexin Capsules, Oral Suspension and Tablets were presented to the EAG.
Members highlighted that a dissolution test would be required for all of the monographs.

Oral Suspension
In addition to the tests in the draft revision for Cefalexin Oral Suspension, the members expressed the need to explore the addition of pH and antimicrobial tests and limits for the monograph.

Identification
Members agreed to the removal of the Identification test B for the Capsules and Tablets monographs as Identification by Infra-red is sufficient, and to replace identification test B for the oral suspension monograph with retention time comparison of solutions 1 and 2 in the Assay.

Identification test A for the Oral Suspension monograph remained drafted as a Thin-Layer Chromatography method due to the difficulties posed by the formulations when considering extraction for Infra-red identification.

Related Substances

The related substances methods in the capsules and tablets monograph had been updated from TLC to HPLC based upon the Ph. Eur monograph. This method was also drafted into the oral suspension monograph.

The EAG agreed that the oral suspension test method should be evaluated by the laboratory and that the tablets and capsules monograph and limits would be subjected to public consultation.

Assay
There was no change to the assay conditions as the published methods were suitable

477 Tylosin Preparations ABS(20)06
Tylosin Injection (Revision)
Tylosin Premix (New)
Tylosin for Veterinary Oral Solution (New)

A revised Tylosin Injection monograph was presented to the EAG based upon the revised monographs for Tylosin, Tylosin Tartrate and Tylosin Phosphate API's in Pharmeuropa supplement 10.0.

Monographs for Tylosin Premix and Tylosin for Veterinary Oral Solution were to be made available for public consultation and published in a future edition of the BP.

Composition and Related Substances
The Secretariat had included the updated Ph. Eur. composition and Related substances test in the draft monographs.

The Secretariat agreed to amend the limit for each individual impurity to 1.0% in line with VICH limits across the monographs.

Tyramine

It was therefore agreed that the test for Tyramine would remain in the Tylosin Injection monograph.

478 Pivmecillinam Tablets (New) **ABS(20)07**

The monographs would be included in a future publication of the BP.

479 Flucloxacillin Preparations **ABS(20)08**
Flucloxacillin Capsules (Revision)
Flucloxacillin Injection (Revision)
Flucloxacillin Oral Solution (Revision)
Flucloxacillin Oral Suspension (Revision)
Co-fluampicil Capsules (Revision)
Co-fluampicil Oral Suspension (Revision)

The Secretariat performed a full review on the product monographs following a revision of the API monograph in the Ph Eur 31.1 review. The product monographs were updated and modernised in line with the current BP policies and style guide and presented to the EAG.

Manufacturers of the Co-Fluampicil products had been contacted to provide methodology suitable for the dual formulations which would be presented to the members at a future meeting of the EAG.

Definition (Oral Suspension)
It was agreed that the Magnesium salt is the only form that should be used for the Oral Suspension.

Identification (All monographs)
The published monographs for Flucloxacillin Capsules and Injection used identification by Infra-red absorption.

The monographs for Flucloxacillin Oral Solution and Oral Suspension were drafted to contain identification by Infra-red absorption, in order to replace the current TLC method and were awaiting suitable extraction procedures from a manufacturer.

The members agreed the laboratory should be asked to confirm the suitability of the Oral Solution, Oral Suspension identification methods.

Dissolution (Capsules and Oral Suspension)
The Secretariat had contacted manufacturers to obtain suitable dissolution tests and acceptance criteria. The members agreed that these methods were to be added to the draft monographs and assessed by the laboratory when received.

Related Substances (All monographs)
An LC procedure based on the Ph Eur Flucloxacillin Sodium draft monograph had been drafted. The methodology was an improvement on published procedures and provided control for a number of additional named impurities and a tighter control for un-identified impurities.

The limits for these monographs had been drafted based on licensed specifications. The EAG confirmed all monographs should be assessed by the laboratory.

Assay (All monographs)
It was agreed that the laboratory would assess the method, which was harmonised with the Related substances method.

The content limits for the individual monographs have been drafted in-line with current policy and licensed specifications.

It was agreed that the Secretariat would investigate the wording of the Injection assay procedure with respect to the new Parenteral Preparations monograph.

IV FOR INFORMATION

480 Out of Stock BPCRS report **ABS(20)09**

An update on the status of out of stock BPCRS relating to the EAG was presented to the members, based on the March 2020 BPCRS update.

481 Work Programme **ABS(20)10**

Additions to the work programme
The Secretariat updated the members with status of monographs that were added to the work programme during previous meetings.
Manufacturers had been contacted to provide data for a number of the monographs and the Secretariat were waiting to receive large data sets for the Levofloxacin and Co-fluampicil product monographs.

Review of Laboratory Queue
The next stage of the ABS monograph improvement work was presented as a review of the monographs waiting for laboratory assessment.

It was agreed that the queue would be subject to a review of the need for laboratory work based on a more elaborate review process.

It was agreed that this review would be presented to the EAG at a future meeting.

482 British Pharmacopoeia Matters **ABS(19)27**

The Secretariat highlighted the recent work of the British Pharmacopoeia including a key update to the BP Website and recruitments within the BP Secretariat.

469 European Pharmacopoeia Matters **ABS(19)28**

An informal report from the 166th meeting of experts Group 7 was presented to the EAG.

There were no monographs for comment on PharmEuropa 32.1 that were under the remit of the EAG. The Secretariat thanked the experts for their support to the UK Delegation.

The products of fermentation general monograph had been reviewed in order to indicate the risk associated with the histamine levels within fish peptone fermentation nutrients.

V ANY OTHER BUSINESS

None.

VI DATE OF NEXT MEETING

Wednesday 23rd September 2020.