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 3 December 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, Mr P Fleming, Dr E Gray, Dr J Lough, Mr D Malpas and Mr S Nolan.

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

Apologies: Dr S Bale.

Dr E Bush, Mr A J Caws, Dr J Lough, and Mr D Malpas declared an interest in one or more agenda items and appropriate action was taken.

INTRODUCTORY REMARKS

573 **Welcome** The Chair welcomed members, Ms K Busuttil and Ms M Nanasi from the BP Laboratory, to the meeting. The Chair introduced Mr R Smith, who had recently joined the BP Secretariat and was attending EAG MC1 for training purposes.

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

574 **General Matters**

The emergency evacuation procedure for 10 South Colonnade was noted.

Declaration of Interests Members were thanked for providing their interests prior to the meeting. Members were reminded to inform the Secretariat of any changes to their interests throughout the year.

575 **BP Update**

Members were provided with an update on BP staff changes, recent topics of discussion by BPC and the progress of BP project activities.

576 **MINUTES**

The minutes and summary minutes of the meeting held on 25 June 2019 were confirmed.

577 **Matters Arising from the Minutes**

Matters arising from the 25 June 2019 meeting were noted and members had no additional comments.

MONOGRAPHS

578 Monograph Portfolio Review

The Secretariat introduced the aim of the project and explained the principles developed to guide the proposals. The approach had been approved by the BP Commission, and recommendations for the omission and revision of MC1 monographs were presented to members following the completion of the first review stage.

578.1 Members endorsed the omission of Clomethiazole, Clomethiazole Edisilate, Clomethiazole Capsules, Clomethiazole Oral Solution, Isradipine Tablets, and Tioconazole Cream from the BP 2021, subject to stakeholder comments and BPC approval.

578.2 Members endorsed the proposal for the revision of 12 monographs to rationalise BPCRS usage, in future editions of the BP.

579 Mycophenolate Mofetil preparations (new):

Mycophenolate Mofetil Capsules
Mycophenolate Mofetil Oral Suspension
Mycophenolate Mofetil for Infusion
Mycophenolate Mofetil Tablets

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

580 Sodium Valproate preparations (revisions):

Sodium Valproate Tablets
Sodium Valproate Prolonged-Release Tablets
Sodium Valproate Gastro-Resistant Tablets
Sodium Valproate Prolonged-Release Capsules
Sodium Valproate Oral Solution

The laboratory evaluations had been completed, following reports of poor extraction from prolonged-release tablet formulations by users.

580.1 **Dissolution – Tablets** The laboratory had found that the chromatographic conditions of the drafted Assay method were applicable to the existing Dissolution method. Members endorsed the inclusion of these conditions in order to harmonise the two tests.

580.2 **Related substances** The drafted methods were found to be suitable for inclusion in the Oral Solution, Prolonged-release Tablets, Prolonged-release Capsules, and Tablets monographs. The Secretariat agreed to publish these revisions and further investigate the method for gastro-resistant tablets.

580.3 **Assay** The drafted methods were found to be suitable for inclusion in the Gastro-resistant Tablets, Prolonged-release Tablets, and Tablets monographs. The Secretariat agreed to publish these revisions and further investigate the method for prolonged-release capsules. The published method was retained for the Oral Solution monograph.

581 Mebendazole preparations (new):
Mebendazole Chewable Tablets
Mebendazole Oral Suspension

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

582 Haloperidol preparations (revisions):
Haloperidol Capsules
Haloperidol Injection
Haloperidol Oral Solution
Strong Haloperidol Oral Solution
Haloperidol Tablets

The Haloperidol family of monographs had been updated with the findings from a report prepared by a University of Sunderland student.

582.1 **Strong Haloperidol Oral Solution** Members agreed with the proposal that the monograph for Strong Haloperidol Oral Solution should be put forward to BPC for omission, on the basis that there were no licensed products and there was no reference to a strong haloperidol oral solution in the BNF.

582.2 **Definition (Oral Solution only)** Members agreed that the strength restriction in the definition should be deleted, subject to confirmation that the Strong Haloperidol Oral Solution would be omitted from the BP 2021.

582.3 **Content (Injection & Tablets)** Members agreed that the content limits should be tightened from 90.0 – 110.0% to 95.0 – 105.0%, subject to stakeholder comments.

582.4 **Characteristics (Oral Solution)** Members agreed the deletion of the non-mandatory characteristic of 'a clear, colourless solution' from the Oral Solution monograph.

582.5 **Identification (Injection & Oral Solution)** Members accepted the replacement of chloroform with dichloromethane in the IR extraction procedure.

582.6 **Identification B (Capsules, Injection & Oral Solution)** Members agreed that a second identification test was not required, as the IR test was sufficiently discriminatory.

582.7 **Dissolution (Capsules & Tablets)** A dissolution procedure had been added to the solid oral dosage form monographs based on the test in the USP monograph for Haloperidol Tablets. Members accepted the tests, subject to confirmation of suitability from stakeholders.

582.8 **Related substances (All)** The Ph. Eur. related substances test had been found suitable for Haloperidol Tablets and Oral Solution. An evaluation of the methods against the available products on the UK market indicated that the methods would be suitable for the capsules and injection monographs.

The following limits were agreed, subject to stakeholder comments:

- Impurity D at NMT 0.5%
- Impurity B at NMT 0.3%
- other secondary peaks at NMT 0.2%
- total impurities at NMT 1.0%
- disregard limit of 0.1%

582.9 **Assay (Injection & Oral Solution)** Members confirmed the conclusion that the LC procedure published in the Capsules and Tablets monograph would be suitable for the Injection and Oral Solution monograph.

582.10 **Impurities (All)** Members endorsed the inclusion of a transparency statement.

583 Esomeprazole preparations (new):
Esomeprazole Gastro-resistant Capsules
Esomeprazole Gastro-resistant Tablets
Esomeprazole Gastro-resistant Granules
Esomeprazole Infusion

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

584 Metformin and Sitagliptin preparations (new):
Metformin and Sitagliptin Tablets
Metformin and Sitagliptin Prolonged-release Tablets

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

585 Dithranol Cream (revision)

585.1 **Content** A request had been received for a reduction in the lower content limit in the monograph from 85.0% to 75.0%.

Members advised that a reduction to the limit should be approved by the national competent authority prior to adoption in the BP monograph.

586 Ranitidine liquid preparations (revisions):
Ranitidine Injection
Ranitidine Oral Solution

Further stability information had been received for the oral solution in support of a request for revision.

586.1 **Related substances (Oral Solution)** The following limits were agreed:

Impurity C at NMT 2.0%
Impurity D at NMT 1.5%
Impurity B at NMT 1.2%
Impurity E and impurity I at NMT 0.5% of each
Impurity A at NMT 0.3%
Any other secondary peak at NMT 0.2%
Total impurities at NMT 5.0%.

Members agreed that there was insufficient justification to increase the “any other secondary peak” limit to 0.3%.

587 Ketoconazole Shampoo (Revision)

The Secretariat presented a proposal for revision to the harmonised Related substances and Assay method, following issues reported by users with the specified HPLC column.

587.1 **Related substances** Members agreed that the revised draft method required laboratory evaluation due to the substantial changes.

587.2 **Impurities** Members noted that impurity 2 was not listed under the Impurities transparency statement, and the Secretariat agreed to include this in line with the nomenclature and structure contained in the Ketoconazole Cream monograph.

588 Fluconazole preparations (revisions):
Fluconazole Capsules
Fluconazole Infusion
Fluconazole Oral Suspension

Related substances Users had reported that a correction factor may be required for impurity B. The lab had found that correction factors of 0.15 and 0.05 should be applied to impurities B and C respectively, and members accepted the laboratory recommendation.

589 Cetirizine Tablets (Revision)

An MAH had requested a revision to the monograph to include a new degradant.

589.1 **Related substances** The Licensing Division informed the Secretariat that the impurity was not specified in the majority of products, and members agreed that further information was required before the impurity would be considered for inclusion.

590 MC1 Work status and updates

The MC1 work programme was presented to members for information.

591 MC1 Out of stock BPCRS review

591.1 The Secretariat noted that the Laboratory were experiencing difficulty obtaining reference materials to support BPCRS standards, and asked members for advice and support in procuring materials.

592 Pharmeuropa Update

The Secretariat presented BP monographs that would require revision in the next publication or addition to the work programme following adoption of the revised monographs presented in Pharmeuropa 31.3 and 31.4.

593 AOB

No items were raised.

594 Date of next meeting

30 June 2020