BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group MC1: Medicinal Chemicals

SUMMARY MINUTES

A meeting of Expert Advisory Group (EAG): Medicinal Chemicals 1 (MC1) was held via videoconference on Wednesday 31 January 2024.

Present: Dr P Marshall *(Chair),* Dr E Bush (*Vice-Chair*), Dr Varada Bapat, Dr J C Berridge, Mr S Boland, Professor D Cairns, Mr A J Caws, Dr J Lough, Mr D Malpas and Dr F Pina.

In attendance: Mr M Whaley, Ms M Dmitriieva, Ms G Li-Ship, Mr S Greatorex (BP Lab).

Apologies: Mr P Fleming, Dr G Lee, Mr S Nolan.

728 INTRODUCTORY REMARKS

Welcome The Chair welcomed the experts to the meeting and extended a particular welcome to two new members, Dr V Bapat & Mr S Boland who were attending their first meeting. All members gave a brief introduction of their background and experience.

Expense Claims Members were asked to note that expenses claims should be submitted electronically to committeeservicesteam@mhra.gov.uk.

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

Declaration of Interests Members were thanked for providing their interests prior to the meeting. Committee Services also reminded members that holding shares in companies in the pharmaceutical industry is an interest that should be declared.

Dr Bapat, Dr Bush and Mr Caws declared interests in one or more agenda items and appropriate action was taken.

MINUTES OF THE PREVIOUS MEETING **MC1(24)1**

729 The minutes and summary minutes of the meeting held on 20 July 2023 were confirmed.

MATTERS ARISING **MC1(24)2**

730 Matters arising and correspondence items from the meeting held on the 20th July 2023 were noted. Members agreed that the potential omission of the BP monograph for Aspirin Effervescent Soluble Tablets should still be raised for consideration by the BP Commission. Members had no additional comments.

REPORTS AND CORRESPONDENCE

731 BP Update **MC1(24)3**

Members were provided with an update on recent BP activities including the review of Expert Advisory Groups, Panels of Experts and Working Parties of the BP Commission,

the update to the BP website and the publication of the latest BP guidance documents (ATMP and Sustainability).

732 Carboplatin Injection **MC1(24)4**

Assay and Impurities Statement The Secretariat had received a request from a user for an update to a query who had made observations and proposals for the revision of the Assay and the Impurities statement in the monograph.

The user had been unable to meet the SST requirement of not less than 5000 plates included in the Assay and the EAG agreed to revise the Assay in this monograph.

Additionally, the user highlighted that the Impurities statement was incorrect and should only include impurity B as this was the only impurity test in the monograph.

Members discussed the column change and the need for the theoretical plates system suitability criteria. Members agreed to delete the requirement for the minimum theoretical plates so that the column change was not needed; however, members asked the Secretariat to confirm the columns that had been used in the assay. Members also endorsed the Impurities section revision.

733 Esomeprazole Gastro-resistant Granules **MC1(24)5**

The Secretariat had received correspondence from a manufacturer based in India proposing revisions to the Dissolution, Related substances and Assay tests.

Dissolution The user suggested revising Solution A as per the USP monograph and to harmonise the concentrations of the sample (0.0002% w/v) and reference standard solutions (0.001% w/v).

Members agreed the Secretariat should harmonise the dissolution sample and reference solution concentrations.

Related substances The user suggested revising Solution A as per the USP monograph and use the USP buffer in mobile phase B preparation to overcome what was reported as the problematic “haziness” of the solution. Members agreed that this issue should be further investigated.

Assay The user suggested revising Solution A as per the USP monograph and to revise the final dilution of the standard solution preparation using solution A.

Impact on other monographs The group discussed if the issues raised impacted other esomeprazole monographs. As the original method was based on validated methods it was agreed that the manufacturer who provided the methods would be consulted and asked to comment.

As part of the review, the Secretariat would collaborate with the manufacturer and provide details on the evolution of the monograph and report back at the next meeting.

734 Metformin and Sitagliptin Tablets **MC1(24)6**

The Secretariat had received a user request to revise the Dissolution method detection wavelength from 255 nm to 205 nm, for sitagliptin determination, citing low area response which affected precision in results.

There was only one UK MAH licensed formulation upon which the Dissolution test was based; the user who sent the request for revision was not a UK MAH. No further complaints had been received from other users.

Members agreed that no action was needed, and the Dissolution test would not be revised.

735 Amlodipine Oral Solution **MC1(24)07**

The Secretariat had been contacted by a BP user who highlighted an issue with the system suitability for the Related substances test, which had been revised in the BP2022.

The Secretariat proposed to correct this monograph for the BP 2025. Members agreed to this proposal.

NEW MONOGRAPHS

736 Alfentanil Injection **MC1(24)08**

The draft new monograph would be included in a future BP publication, subject to laboratory evaluation and stakeholder comment.

NEW MONOGRAPHS IN PROGRESS

737 Aripiprazole Preparations: **MC1(24)09**

Aripiprazole Tablets – draft monograph
Aripiprazole Orodispersible Tablets - draft monograph
Aripiprazole Oral Solution - draft monograph

The draft new monographs would be included in a future BP publication, subject to laboratory evaluation and stakeholder comment.

738 Levetiracetam Preparations: **MC1(24)10**
Levetiracetam Sterile Concentrate – draft monograph
Levetiracetam Infusion – draft monograph
Levetiracetam Tablets – draft monograph
Levetiracetam Granules – draft monograph

The draft new monographs would be included in a future BP publication, subject to laboratory evaluation and stakeholder comment.

739 Tramadol Preparations: **MC1(24)11**
Tramadol Soluble Tablets
Tramadol Dispersible Tablets
Tramadol Orodispersible Tablets

The draft new monographs would be included in a future BP publication, subject to laboratory evaluation and stakeholder comment.

REVISION OF MONOGRAPHS

740 Azathioprine Tablets **MC1(24)12**

A revised monograph for Azathioprine Tablets had been drafted based on validated methods and data submitted by a collaborating manufacturer. Minor technical and editorial comments that were made by members would be considered as agreed in the meeting.

Identification The HPLC Assay method had been drafted, based on the MAH method and it had been proposed that the UV spectrum comparison and the retention time of the principal peak from the Assay test could replace the existing TLC and precipitate colour tests. Members agreed the BP Laboratory should be asked to evaluate the proposed method.

Dissolution The method presented to the group had been drafted based on the MAH method and the members agreed the BP Laboratory should be asked to evaluate the UV method with the proposed Q limit of 75% in 30 minutes.

Related substances The drafted method presented to the EAG was an isocratic HPLC method based on a collaborating MAH method which controlled impurities B and C. The members agreed the BP Laboratory should be asked if Ph.Eur. impurity A (a process/synthetic impurity) can be controlled, when evaluating this method.

Members recommended that the list of impurities including Ph.Eur. impurities (C, E and F) as well as impurity 1 (5-hydroxy-1-methyl-4-nitroimidazole) were investigated for the next draft of this monograph. The Laboratory were to be asked to investigate any correction factors as well as to recommend a system suitability test.

Assay The isocratic HPLC method had been drafted based on the collaborating MAH method to replace the non-specific UV test. The members agreed the BP Laboratory should be asked to evaluate the suitability of this method and asked that the potential of degradation caused by ultrasound or heating could be investigated, although validation data from the MAH did not indicate any problems.

BPCRS review Established EPCRS and BPCRS can be used to support this monograph and had been included in the draft revised monograph.

741 Nifedipine Preparations: **MC1(24)13**
Nifedipine Capsules – draft monograph
Nifedipine Prolonged-release Capsules – draft monograph
Nifedipine Prolonged-release Tablets – draft monograph

At the July 2022 meeting, it had been agreed that the test in the Capsules monograph for Nitro- and nitroso-phenylpyridine analogues test should be renamed Related substances to harmonise with the Prolonged-release Capsules and Prolonged-release Tablets monographs and include impurity limits. Other differences between the monographs had been noted and the Secretariat had presented the review to the EAG.

Minor technical and editorial comments made by members would be considered as agreed in the meeting.

Related substances Chromatographic Conditions The Secretariat had compared the chromatographic conditions and suggested amending the mobile phase of the Nifedipine Capsules to harmonise with the Prolonged-release Capsules and Prolonged-release Tablets, replacing the buffer with water. The other recommendation was to harmonise the column length to 15 centimetres for the Capsules and Prolonged-release Tablets.

Members endorsed the changes to these monographs.

Related substances Limits Only the current drafted Capsules had a limit for the "sum of all secondary peaks" at not more than 2.0%. Members agreed that this limit could be used to harmonise the other two monographs although it was suggested that the Secretariat could investigate the specifications or contact MAHs.

It was agreed by the EAG that the limit for Impurity A of NMT 0.5% will be maintained in the drafts to be shared for public consultation.

742 ***EUROPEAN PHARMACOPOEIA*** **MC1(24)14**

Experts were presented with a list of Ph Eur draft monographs that were published in Pharmeuropa 35.4. There was only one draft monograph, Doxapram Hydrochloride Monohydrate, that was related to MC1.

For the Pharmeuropa 36.1 revision, there were 14 texts related to MC1, for which the deadline for comments were still open.

ANY OTHER BUSINESS

743 Work Programme **MC1(24)15**

The Secretariat presented a copy of the current MC1 programme to the Expert Advisory Group. The monographs being targeted for the BP 2025 and BP2026 publications were highlighted.

744 BPCRS Update **MC1(24)16**

The Secretariat provided an update on the BPCRS reports since the last meeting. There were no out-of-stock BPCRSs for any active MC1 monographs.

NEXT MEETING

The next meeting was planned to be an in person in July 2024.