6 December 2016

BRITISH PHARMACOPOEIA COMMISSION
EXPERT ADVISORY GROUP (EAG): MEDICINAL CHEMICALS 1 (MC1)

SUMMARY MINUTES

A meeting of Expert Advisory Group (EAG): Medicinal Chemicals 1 (MC1) was held at 151 Buckingham Palace Road, London SW1W 9SZ on Tuesday, 6 December 2016.

Present: Professor A G Davidson *(Chairman),* Professor D Cairns *(Vice-chairman),* Dr M Ahmed, Dr J C Berridge, Dr E Bush, Mr A J Caws, Mr P Fleming, Mr A James, and Mr D Malpas.

Apologies: Mr M Broughton and Dr J Lough.

In attendance: Mrs M Barrett, Ms H Corns, Ms F Lee, Ms C Galdino, Ms R Lloyd-Williams and Ms M-L Wall.

438 Welcome

The Chairman welcomed everyone to the meeting especially Dr A Gleadle, a lay member of the BP Commission, Ms M-L Wall on secondment to the Secretariat and Ms F Lee, Ms C Galdino and Ms R Lloyd-Williams from the BP Laboratory.

Mrs Barrett was retiring at the end of 2016. As this was her last meeting with the EAG, Professor Davidson thanked her on behalf of MC1 for her considerable support and contribution to the expert group over the years and wished her well in her retirement.

I GENERAL MATTERS

439 Minutes

The minutes and summary minutes of the meeting held on 6 June 2016 were confirmed.

440 Emergency evacuation procedure

The emergency evacuation procedure for Buckingham Palace Road was noted.

441 Declaration of interests

Mr D Malpas, Prof D Cairns and Mr A Caws declared interests in one or more agenda items and appropriate action was taken.

II MATTERS ARISING FROM THE MINUTES

442 Matters arising

A list of 'Matters Arising' from the minutes of the meeting of EAG: MC1 held in June 2016 and those outstanding from previous meetings was presented.

443 MC1 status report
The status report was presented to members for information.

III NEW MONOGRAPHS
444 Repaglinide Tablets

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

445 Prolonged-release Diltiazem Capsules
The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

IV MONOGRAPHS IN PROGRESS

446 Pantoprazole Preparations:
Pantoprazole for Injection
GR Pantoprazole Tablets

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

447 Amlodipine Preparations:
Amlodipine Oral Solution
Amlodipine Tablets

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

448 Metformin & Sitagliptin Tablets

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

449 Sitagliptin and Prolonged-release Metformin Tablets

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

450 Celecoxib Tablets

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

451 Ritonavir Preparations:
Ritonavir Oral Solution
Ritonavir Tablets

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

V REVISION OF MONOGRAPHS AND REPORTS AND CORRESPONDENCE

452 Paracetamol Capsules

BP Commission had proposed that stakeholders were consulted on the inclusion of two dissolution tests in the monograph, one for hard shell and one for soft gel capsules. The test for the hard shell product would retain the current dissolution medium and the soft gel product would include a test with 0.1M hydrochloric acid. No comments had been received on the draft revised monograph. Members agreed, that in the absence of any adverse comments, the revised monograph would be published in a future edition of the BP.

453 Prolonged-release Diltiazem Tablets

Following the meeting in June 2016 the revised draft monograph was posted on the BP website for comment. No comments had been received and it was agreed that the revised monograph would be published in a future publication.

454 Digoxin Preparations:
Digoxin Injection
Digoxin Tablets

Members agreed to defer this item to the next meeting due to time constraints.

455 Co-dydramol Tablets

A request for revision to the BP monograph had been received to accommodate the different ratios of paracetamol to dihydrocodeine which were available on the UK market. The revision was agreed in principle, however, investigation to determine whether the tests in the monograph were suitable for a higher ratio of dihydrocodeine was considered necessary prior to publication of a revised monograph. Replacement of chloroform would also be investigated.

456 Loperamide preparations:
Loperamide Capsules
Loperamide Tablets
Orodispersible Loperamide Tablets

An investigation was underway to determine whether *acetate buffer solution pH 4.7* which included carbon tetrachloride and chloroform in the preparation could be replaced by *acetate buffer Solution pH 4.7 R1*. Members agreed that the monographs would be revised if the alternative buffer could be used as a substitute.

457 Ranitidine preparations:
Ranitidine Injection
Ranitidine Oral Solution
Ranitidine Tablets
Effervescent Ranitidine Tablets

Ranitidine Injection – Related substances limits The following proposed revision to the impurity limits were agreed subject to stakeholder consultation:
impurity A NMT 0.5%,
impurity B NMT 1.0%,
impurity D NMT 1.5%,
impurity F NMT 0.5%,
impurity G NMT 0.5%,
an unknown at RRT 0.5 NMT 0.5% and
an unknown at RRT 1.2 NMT 0.5%,
any other secondary peak at NMT 0.2%
and total impurities NMT 3.0% excluding A, B and D.

It was agreed that information regarding the identity of the unknown impurities should be sought.

Ranitidine Oral Solution – Related substances limits The following proposed revision to the impurity limits were agreed subject to stakeholder consultation:
impurity A NMT 0.5%,
impurity B NMT 1.0%,
impurity C NMT 1.5%,
impurity D NMT 0.5%,
impurity I NMT 0.5%,
any other secondary peak at NMT 0.2%
and total impurities limit of NMT 0.5% excluding A, B, C, D and I.

Ranitidine Tablets – Related substances limits No adverse comments had been received on the proposed revised limits during the public consultation 1 Jan to 31 March 2016. Members agreed that the revised limits as drafted should be published.

Effervescent Ranitidine Tablets – impurity A A revised limit of not more than 0.5%, in line with the limit in the Ph. Eur. Ranitidine Hydrochloride monograph, was agreed.

458 Alkylsulfonate Esters:
Production Statements in BP Monographs

Members agreed that the Secretariat should submit a proposal to the BP Commission to include a production statement regarding formation of genotoxic impurities in product monographs of alkane sulfonate salts, as a prudent safeguard. Appropriate wording of such a production statement and the circumstances under which it should be applied would be considered.

459 Gastro resistant Bisacodyl Tablets

Members agreed to progress this item by correspondence in advance of the next meeting, due to time constraints.

The following actions were agreed by correspondence. Members agreed that data justified:

- an increase in the final stage sampling time from 45 minutes to 60 minutes in the Dissolution test;
- increased limits for impurity A to 0.8% and impurity C to 1.5%.

Impurity A and C were excluded from the total impurity limit, which as a result was decreased from 1.0% to 0.5%. Members agreed, that in the absence of adverse comments, the revised monograph would be published in a future edition of the BP.

460 Pyrimethamine Tablets

Members agreed to defer this item to the next meeting due to time constraints.

461 Prolonged-release Sodium Valproate Tablets

Members agreed to defer this item to the next meeting due to time constraints.

462 Caffeine Citrate preparations:
Caffeine Citrate Injection
Caffeine Citrate Oral Solution

Members agreed to progress this item by correspondence in advance of the next meeting, due to time constraints.

Members confirmed by correspondence that the draft revised monographs should be published in a future edition of the BP.

463 Clonidine Injection

Members agreed to progress this item by correspondence in advance of the next meeting, due to time constraints.

Members confirmed by correspondence that the minor changes to the draft revised monograph should be published in a future edition of the BP.

464 Test for Assay based on Uniformity of content results

Members were asked to note this item, due to time constraints, which was presented for information.

465 Doxepin Capsules

Members agreed to progress this item by correspondence in advance of the next meeting, due to time constraints.

Members confirmed by correspondence that the correction factor applied to impurity B in the Ph Eur monograph for Doxepin Hydrochloride should be applied in the Doxepin Capsules monograph, as the two methods were harmonised.

466 Cisplatin Injection

Members agreed to progress this item by correspondence in advance of the next meeting, due to time constraints.

The following was agreed by correspondence. Members agreed that data provided justified an increase in the limit for impurity A to 2.0%. A decrease of the limit for impurity B from 3.0% to 1.5% was considered acceptable provided that this did not impact manufacturers. Members agreed, that in the absence of adverse comments, the revised monograph would be published in a future edition of the BP.

VI Any Other Business

467 Piperonyl Butoxide (BP Vet) for information
Members would be informed about this item by correspondence due to time constraints.

468 Propofol Injection
Members agreed to defer this item to the next meeting due to time constraints.

469 Dates of 2017 meetings
Thursday 8 June and Tuesday 5 December