BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group: Medicinal Chemicals 3

SUMMARY MINUTES

A meeting of this Expert Advisory Group was held at 151 Buckingham Palace Road, London SW1W 9SZ on Wednesday 25th February 2014.

Present: Mr V Fenton-May (*Chairman*), Professor E Williamson (*Vice-chairman*), Professor M Almond, Mr S Arkle, Mr C T Goddard, Dr K Pugh, Dr B Rackstraw, Dr R Torano, Mr M Tubby.

In attendance: Prof. K Taylor, Mr A Evans, Ms H Corns, Mr N Patel, Ms M Nanasi.

Apologies: Mr P Hampshire, Mr I R Williams.

INTRODUCTORY REMARKS

The Chairman welcomed Professor Matthew Almond, a new member of the EAG; Professor Kevin Taylor, the new Chair of the BP Commission attending as an observer to the meeting; Mr Nimesh Patel and Ms Marta Nanasi attending on behalf of the BP Laboratory.

The Chairman reminded members that Ms Harjit Jagpal should be contacted if members experienced any difficulties with their travel bookings or expenses claims.

The Chairman reiterated to members the confidential nature of the papers presented at EAG meetings and that members should declare any interests at the start of each agenda item.

I MINUTES

The minutes and summary minutes of the meeting held on 25th September 2013 were confirmed.

II MATTERS ARISING FROM THE MINUTES

371 The following matters arising from the meeting held on 25th September 2013 were noted.

Climatic Zones The Secretariat reported that the issue of applying limits to cover different climatic zones, raised by MC3, had been discussed by the BP Commission in December 2013. Members of the BP Commission had considered whether to retain the current strategy of applying limits based on approved UK products, or whether to include wider or multiple limits to assist manufacturers supplying products in other climatic zones. It was agreed that further investigation should be carried out before a final policy recommendation was made.

Monograph Titles Members were informed that the use of Clobetasol Scalp Application as a monograph title had been referred to EAG NOM for consideration. The EDQM standard term for the pharmaceutical form was Cutaneous Application, however Scalp Application rather than Cutaneous Application had been used in BP monograph titles.

Systematic Names for Impurities The Secretariat informed members that the systematic names and structures of the impurities to be included in the monographs for Clobetasol, Ursodeoxycholic acid, Fluticasone and Salmeterol had been provided to EAG NOM for review.

Fluticasone and Salmeterol Inhalation Powder, pre-dispensed and Pressurised Inhalation Since the previous EAG meeting, the Secretariat had received a data package for Fluticasone and Salmeterol Pressurised Inhalation.

Hydroxyzine Oral Solution The Secretariat was awaiting further information before proceeding with the revision of this monograph.

III REPORTS AND CORRESPONDENCE

372 Members' details MC3(14)1

Members were asked to check the contact details listed and to inform the Secretariat of any amendments required.

373 British Pharmacopoeia Chemical Reference Substances MC3(14)2

The British Pharmacopoeia Chemical Reference Substances approved since the last meeting of the EAG were noted.

374 Emergency Procedures MC3(14)3

A copy of the 151 Buckingham Palace Road Evacuation Procedures was provided to members for information.

375 EAG Work Programme MC3(14)4

A copy of the work programme for EAG: MC3 was provided to members for information. Members were asked to contribute data should they have an interest in any of the products.

376 BP Updates MC3(14)5

The Secretariat provided members with an update on changes within the MHRA and the BP.

377 Anti-epileptic Drugs MC3(14)6

Members were informed that the MHRA had released guidance in November 2013 regarding the interchangeability of anti-epileptic drugs (AEDs). The Committee on Human Medicines (CHM) had reviewed evidence on patients switching between different manufacturers products and had concluded that, whilst there was no clear evidence of harm associated with switching products, an effect on some patients could not be ruled out. CHM had grouped AEDs according to whether a patient should be maintained on a specific product. For category 1 AEDs, CHM advised the maintenance of the patient on a specific product; for category 2 AEDs, a clinical judgement was required as to whether a patient could change between different manufacturer's products and for category 3 AEDs, the advice was that it was usually unnecessary to maintain patient on a specific product. Advice was sought from members on whether an opening statement should be included in the BP monographs for category 1 (not interchangeable) and category 2 (may be interchangeable) AEDs. Members were content to follow the direction of the BP Commission regarding the inclusion of an interchangeability statement in BP monographs for AED products.

IV NEW MONOGRAPHS

378 Gabapentin Oral Solution MC3(14)7

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

379 Pramipexole Tablets and Prolonged-release Tablets MC3(14)8

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

380 Sildenafil Preparations: MC3(14)9

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

V MONOGRAPHS IN PROGRESS

381 Estradiol Preparations MC3(14)10

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

382 Gabapentin Capsules MC3(14)11

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

383 Gabapentin Tablets MC3(14)12

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

384 Vecuronium Bromide Injection MC3(14)13

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

VI REVISION OF MONOGRAPHS

385 Beclometasone Aqueous Nasal Spray MC3(14)14

A BP user had contacted the Secretariat to ask whether they could claim compliance with the BP if their product contained Beclometasone Dipropionate Monohydrate instead of Anhydrous Beclometasone Dipropionate as specified in the published monograph. It was found that both APIs were used in beclometasone aqueous nasal sprays. It was proposed that the definition in the monograph was revised to allow for both forms of the API to be controlled by the monograph. Members agreed to accept the proposed change.

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

386 Benzydamine Oromucosal Spray & Benzydamine Mouthwash MC3(14)15

An error had been identified in the chromatographic conditions by a BP user. It was agreed that the correction to the conditions would be made.

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

387 Budesonide Pressurised Inhalation MC3(14)16

A BP user had contacted the Secretariat with a request to double the concentration of solution (3) in the Related substances test as they had been unable to meet the signal to noise requirement. The company had provided data to support the revision. Members agreed to accept the proposed revision. The Secretariat noted that all Budesonide product monographs contained this requirement and it was agreed that the amendment should be applied to all Budesonide preparation monographs.

It was noted that it was unusual to prepare a pressurised inhalation sample for Related substances as

described in the test, as a more standard approach was to freeze the canister to obtain the material. The Secretariat agreed to amend the wording of solution (1) to read 'Freeze the pressurised container and carefully open the canister. Dissolve a quantity of the frozen contents containing 2 mg of Budesonide…'

The Secretariat had received data from a manufacturer containing validation for the reduction in the concentrations of the solutions used for the Assay. This was to allow the Assay to be used with the lower strength products manufactured by the company. The Secretariat noted that the Assay solution concentrations in Budesonide Inhalation Powder, pre-dispensed were also unsuitable for all of the commercially available products. Members agreed that the data supported the proposed revision to the Assay and that the change should be applied to the two monographs.

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

388 Colecalciferol Preparations MC3(14)17

The Secretariat had been contacted by a manufacturer of Colecalciferol Tablets. The manufacturer indicated that pre-colecalciferol should be included in the Assay calculation. Members agreed to the proposed revision and identified that the Colecalciferol Preparation monographs would benefit from an update.

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

389 Domiphen Bromide MC3(14)18

The Secretariat were contacted with a request to increase the upper limit of the melting point test from 116°C to 119°C and had received data to support the revision. Members accepted that the data supported the proposed revision but concluded that wider limits reduced the stringency of the test. Members agreed that Identification tests A-C would be sufficient for this product and that Identification D should be omitted from the monograph.

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

390 Iron Sucrose Injection MC3(14)19

A manufacturer had requested that this monograph was revised in-line with the USP monograph and had provided data to support such a revision. Members recommended that the proposed revisions were adopted.

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

391 Morphine Preparations MC3(14)20

391.1 The Secretariat had received a report of an analyst experiencing problems with the Related substances test in the Morphine Tablets monograph. Upon review, the Secretariat had identified all Morphine preparation monographs would benefit from an update. Members agreed that revision of the Morphine product monographs should be investigated and may be included in a future BP publication, subject to comments from manufacturers.

392 Nitrazepam Preparations MC3(14)21

The Secretariat had received a number of questions from BP users on how to acquire Nitrazepam impurity A as EDQM was no longer supplying it as a reference standard. Upon review, the Secretariat had identified that the methods in the Ph. Eur. monograph for Nitrazepam had been updated and that

the BP Nitrazepam preparation monographs would benefit from an update as well. Members agreed that revision of the Nitrazepam product monographs should be investigated and may be included in a future BP publication, subject to comments from manufacturers.

393 Prednisolone Tablets **MC3(14)22**

The Secretariat had received a query from a user regarding the purpose of some of the solutions in the Assay for Prednisolone Tablets. The Secretariat had identified that the LC procedure specified the use of an internal standard. Members agreed that the removal of internal standards from LC methods would be an improvement and recommended that the Secretariat investigated removal of the internal standard from the monograph.

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

394 Preparations Containing Chloroform **MC3(14) Supp.**

Members agreed to amend those monographs in the BP for pharmaceutical preparations that contained chloroform above the acceptable daily intake (ADI) of 10 µg/kg. Potential options of revising/omitting the affected monographs were discussed. Members agreed that the removal of extemporaneous preparation instructions from monographs where a licensed product was available could be an effective means of implementing this change.

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

VII EUROPEAN PHARMACOPOEIA COMMISSION

Members were directed to log-in to the BP website to view the latest text from the Ph. Eur.

VIII ANY OTHER BUSINESS

Members agreed that the new style of compiling the papers for the meeting was an improvement.

Date of Next Meeting
Tuesday 7th October 2014.