+2577m/SW/1

COMMERCIAL IN CONFIDENCE CSM/90/2nd Meeting

NOT FOR PUBLICATION

COMMITTEE ON SAFETY OF MEDICINES

MINUTES OF MEETING HELD ON WEDNESDAY 21 FEBRUARY 1990 AT 1PM AND THURSDAY 22 FEBRUARY 1990 AT 9.00 AM IN THE 19TH FLOOR CONFERENCE ROOM MARKET TOWERS

Present

Professor A W Asscher (Chairman)
Professor C L Berry +
Professor S S Bleehen
Professor T G Booth
Professor A M Breckenridge
Professor A T Florence
Professor E Gordon-Smith
Professor F Harris
Professor H S Jacobs O
Dr W A Jerrett
Professor D H Lawson
Professor M J S Langman
Mr F E Loeffler O
Dr S A Montgomery
Professor M D Rawlins
Dr D A J Tyrrell O
Professor M P Vessey O
Dr D Jefferys (Medical Assessor)
Dr S Wood (Medical Assessor) (Adverse Reactions)
Dr J Purves (Pharmaceutical Assessor)
Mr J Bewley (Secretary)
Mr L R Whitbread (Assistant Secretary)
Dr G Bem O
Dr B Davis +
Dr J Dunne +
Dr S Fawcett
Dr K Fowler
Dr J Hilton
Dr R Lee
Mr M McGovern +
Dr A Nath
Dr J Ritchie +
Dr F Rotblat
Dr R Shah O
Dr J Sims
Mr H Stemplewski O
Dr L West O
Dr P Waller O

Guest Member

Professor J G Collee O

Also Present

Mr A Stewart
Mr Mark Bratton
Dr K Winship
Mrs M Dow
Ms J Viner +
Ms A M Pittaway O

+ 21 February 1990 only

O 22 February 1990 only

1. Apologies and Announcements

1.1 The Chairman reminded the Committee that the papers and proceedings were confidential and should not be disclosed.

1.2 Apologies had been received from Professors McLean, Midgley, Drs Finch, and Oakley for both days, from Mr Loeffler, Professor, Vessey and Dr Tyrrell for 21 February and Professor Berry for 22 February and Professor Langman for the afternoon of 22 February.

1.3 The Committee were informed that April would be a one day meeting on Thursday 26 April 1990.

1.4 The Chairman welcomed Professor Collee as a member for the day on 22 February.

2. Minutes of the Meeting held on 25 January 1990

The minutes were agreed and signed by the Chairman as a true record of the meeting.

3. Matters Arising

None.

4. Applications

4.1 PL 0286/0116: SYNAREL NASAL SPRAY: SYNTEX

4.1.1 Professor Jacobs declared a personal specific interest, but answered questions from the Chairman. Professor Florence declared a personal non-specific interest. Neither took part in the decision. Dr Montgomery declared a non-personal non-specific interest but this did not debar him from taking part in the decision.

4.1.2 The Committee noted Tabled Paper IV.

4.2 PL 0034/0292-0294: STARRILL TABLETS: E R SQUIBB AND SONS
PL 0034/0291 : CAPTON TABLETS : E R SQUIBB AND SONS

Professor Booth declared a personal non-specific interest and took no part in the decision.

4.3 PL 0012/0214: PENTACARINET 300 mg: MAY AND BAKER

4.3.1 The Committee requested that the Company should be asked to provide a user package insert for the benefit of the medical personnel with regard to the procedures to be used in the safe administration of the product.

4.3.2 The decision on the application was deferred until receipt of the user package insert.

4.4 PL 0032/0153: PROVERA TABLETS: UPJOHN

4.4.1 Professor Bleehen declared a non-personal non-specific interest, but this did not debar him from taking part in the decision.

4.4.2 The Committee decided that as a matter of urgency the Oral Contraceptives Working Party (renamed the Safety of Steroid Hormone Treatment Working Party) should be re-convened to address the question of hormone replacement therapy and the risk of breast cancer in particular.

4.4.3 The Committee instructed the Secretariat to convey to the Company informally the Committee's views, namely that there was insufficient data to assess efficacy of the product in the dosage proposed and that they would wish to consider the question of safety for long term usage following the Working Party report.

4.5 PL 0001/0145: ESTRAPAK 50: CIBA-GEIGY

Professor Vessey declared a non-personal non-specific interest, but this did not debar him from taking part in the decision.

4.6 PL 0032/0152: PROSTIN 15m: UPJOHN

Professor Bleehen declared a non-personal non-specific interest, but this did non debar him from taking part in the decision.

4.7 PL 0071/0330-1: DOMPERIDONE TABLETS: STERLING WINTHROP

Professor Rawlins declared a non-personal non-specific interest, but this did not debar him from taking part in the decision.

4.8 PL 0010/0163: KOATE HS: BAYER

Professor Langman declared a personal non-specific interest and took no part in the decision.

5. Written Representations

The Committee considered the following:-

5.1 PL 0337/0123: IBUPROFEN AND CODEINE TABLETS : NAPP

5.2 PL 0337/0116: T M INHALER : NAPP

5.3 Professor Florence declared a personal non-specific interest and took no part in either decision.

5.4 The Committee's advice and reasons for that advice, are given at Annex B.

6. Hearings

The Committee considered the following:-

6.1 PL 0286/0110-11: TORADOL IM: SYNTEX

6.1.1 Professor Florence declared a personal non-specific interest and took no part in the decision. Dr Montgomery declared a non-personal non-specific interest, but this did not debar him from taking part in the decision.

6.1.2 The Committee noted Tabled Paper I.

6.2 PL 0095/0211-0213: SUPRAX TABLETS AND SUSPENSION: CYANAMID

6.2.1 The Committee noted Tabled Papers V and VI.

6.2.2 The Committee agreed that a Chairman's letter should be sent to the Company, stating how impressed the Committee was by the rigorous analysis performed and the sound judgement shown by the Company's expert microbiologist.

6.3 PL 0298/0003: INFLUDO: WELEDA (UK) LTD

6.3.1 The Committee noted Tabled Paper III and agreed to defer the Hearing to 29 March 1990.

6.4 The Committee's advice and reasons for that advice and given at Annex C.

7. Role of the Rapporteurs

The Committee noted this paper.

8. Radiopharmaceuticals - Draft European Guidelines

The Committee noted this paper and were asked to send comments to Dr B Matthews by the end of March 1990.

9. The Role of the Hospital Pharmacist in the Reporting of Adverse Drug Reactions and the proposal for a Pilot Study of Adverse Reactions reporting by Hospital Pharmacists in the Northern Region

9.1 The Committee noted these papers and following assurances that i) hospital pharmacists would be able to discuss with their medical colleagues before submitting the reports and ii) that a mechanism had been established for identifying these reports separately on the ADR data base, the Committee endorsed the recommendation for a pilot study - as detailed in Professor Rawlins' paper - of adverse reactions reporting by hospital pharmacists in the Northern Region.

9.2 This matter should be added to the Secretary's Progress report.

9.3 The Committee also noted Professor Booth's report on his studies with community pharmacists.

10. The provision of Plasma Pool Samples for the Control Testing of Blood Products

The Committee noted the paper and endorsed the Biologicals Sub-Committee recommendation that:-

10.1 In view of the limitations of testing for HB_SAg and antibodies to HIV in finished products and the greater sensitivity of tests on the plasma pool, manufacturers should be required to submit formally to NIBSC samples of plasma pools in addition to other samples and protocols required for batch release.

10.2 Product licence holders should be asked to confirm that all plasma pools used in the preparation of a given product have been tested and found to be free of HB_SAg and antibodies to HIV and the licence amended accordingly.

11. Categorisation of Medicinal Products for use in Pregnancy - European Guidelines

11.1 The Committee noted the paper and were concerned about the recommendations.

11.2 Dr Wood invited the Committee to send comments to her so that she would be better placed to argue the UK position in Europe.

12. Desensitising Vaccines and Tabled Paper VII

12.1 The Committee noted the paper.

12.2 The Committee concluded that on available evidence:-

12.2.1 They were unable to advise shortening of the period of observation of patients to less than 2 hours following an injection.

12.2.2 They endorsed their previous advice of August 1986, namely

12.2.2.1 Treatment of patients should only be carried out where full facilities for cardiopulmonary resuscitation are immediately available.

12.2.2.2 Special care should be taken in the treatment of patients with asthma as they may be more susceptible to severe adverse reactions.

12.2.2.3 Patients should be kept under observation for at least 2 hours after treatment.

13. Prescription Event Monitoring of Nabumentone (Relifex)

The Committee noted this information paper.

14. Should B-I Selective Blockers be indicated in patients with respiratory disorders? and Tabled Papers VII and X

The Committee noted the papers and endorsed the draft Current Problems article.

15. Inverted Black Triangle on Promotional Material and Tabled Paper VII

15.1 The Committee considered the paper and strongly endorsed the recommendations to improve the impact of the inverted black triangle symbol on promotional material as follows:-

15.1.1 The inverted black triangle should be printed adjacent to the product name in the body of the advertisement.

15.2.1 The size of the symbol should be as follows:

15.2.1.1 For large full page advertisements, eg in Pulse or GP: 7.5mm sided triangle.

15.2.2.2 A4 size page: 5mm sided triangle.

15.2.3.3 Smaller pages, eg MIMS: 3mm sided triangle.

15.3 A second inverted black triangle symbol should be printed adjacent to the heading of the section headed "Abbreviated Prescribing Information" with the statement "SPECIAL REPORTING TO CSM REQUIRED" adjacent to the symbol.

15.4 The Committee agreed that the Chairman should write to the ABPI with the Committee's conclusions and that the matter should be discussed at the joint CSM/ABPI meeting on March 8, 1990.

16. Beta2 Mimetics, Theophylline and Hypokalaemia and Tabled Papers VII and XI

The Committee noted the paper and endorsed the draft Current Problems article with modifications.

17. Update on Fenoterol and Risk of Death in the UK and Tabled Paper VIII

17.1 The Committee noted the papers and concluded that because of:-

a. differing prescribing practice with respect to fenoterol in New Zealand

b. population differences in New Zealand

c. the historical nature of the data in case control studies ie these relate to events 10 years ago

d. the New Zealand Licensing Authority had not taken regulatory action against the licence and

e. no evidence in the UK of a safety problem

it did not feel that there was any need for regulatory action in the UK at the present time.

17.2 Professor Vessey asked the Secretariat to look into the differences in bioavailability and potency between fenoterol and salbutamol and other bronchodilators and to report back to the SEAR Sub-Committee and the Main Committee. Members agreed.

18. Triazolam: Psychiatric Adverse Reactions and Tabled Paper VII

The Committee noted the paper and endorsed the SEAR Sub-Committee recommendation that:-

18.1 The case, based on the evidence presented, must be judged as not proven, either for or against the drug. Nevertheless, there was a strong signal that triazolam may produce more frequent neuro-psychiatric ADRs than other benzodiazepines.

18.2 The company should be asked to reanalyse the EMIC study.

18.3 Dr Montgomery requested that Upjohn be asked to bring their data sheet into line with other benzodiazepines and with the CSM's recommendations of 1988. The Secretariat agreed to pursue.

18.4 The Company should be asked to consider conducting a comparitive study to investigate the frequency of neuro-psychiatric problems with triazolam compared with other benzodiazepines.

19. The Safety of Nebuliser Solutions

The Committee noted this information paper and thanked Miss R Coulson for her summary of the position.

20. Annual Meeting between CSM and ABPI and Tabled Paper IX

20.1 The Committee noted the papers and agreed that the Chairman, Professors Rawlins, Breckenridge and Dr Tyrrell and Professor John Carless of CPS (due to the unavailability of Professors Florence, Midgley and Booth) would represent CSM and that Drs Jefferys, Wood, Purves and Mr Bewley would represent the Secretariat.

20.2 The Committee also endorsed the following items for the agenda.

a. Introduction by Professor Asscher followed by a presentation from Professor Rawlins and Dr Jefferys on UK applications.

b. Matters arising from last meeting.

c. Current status of licensing procedures:-

i. expert reports
ii. hearings
iii. delays in obtaining product licences

d. Notification of ADR Medico Pharmaceutical Forum booklet.

e. Steps to improve ADR reporting:-

i. yellow card and company communications
ii. black triangle scheme
iii. completion of ADR forms by companies
iv. ADR reporting by hospital pharmacists

f. Categorisation of medicinal products for use in pregnancy.

20.3 Members were also asked to submit any further items for discussion to the Secretary.

21. BSE Working Party Minutes of 10 January 1990

The Committee noted the minutes of the Working Party. A note of Professor Collee's oral report to the Committee is at Annex D.

22. Eosinophilia-Myalgia Syndrome Associated with L-Tryptophan containing products

22.1 Dr Montgomery declared a non-personal non-specific interest, but this did not debar him from taking part in the decision.

22.2 The Committee noted the papers and endorsed the SEAR sub-committee recommendation, that L-Tryptophan had modest efficacy in mild to moderate depressive illness and that no regulatory action was necessary in the UK at the present time.

23. Litigation-Mianserin and Factor VIII

The Committee noted the paper on Mianserin and Mr Bratton's oral report on Factor VIII litigation.

24. Genotoxicity Studies of Gastric Acid Inhibiting Drugs

The Committee noted this item, which would be placed on the Secretary's Progress Report.

25. Secretary's Progress Report

This item was noted.

26. Any Other Business

Mr Bewley informed the Committee that a record 19,246 yellow cards had been received in 1989.

27. Date and Time of Next Meeting

Thursday 29 March 1990 at 10.00 am.

GRO-C

29/3/90