CSM/mins/84/10

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20/12/84

NOT FOR PUBLICATION

COMMERCIAL IN CONFIDENCE

Minutes of the meeting held on Thursday 22 November 1984 in the 19th Floor Conference Suite Market Towers.

Present

Professor Sir Abraham Goldberg (Chairman)
Professor A W Asscher
Dr D Bangham
Professor A M Breckenridge
Professor J W Dundee
Professor P H Elworthy
Professor A T Florence
Professor D G Grahame-Smith
Professor M W Greaves
Dr J M Holt
Professor D Hull
Professor J O'D McGee
Dr B L Pentecost
Professor M D Rawlins
Dr J W G Smith
Professor M P Vessey
Dr D M B Ward
Professor H K Weinbren

Dr R Mann (Medical Assessor)
Dr J Calderwood (Pharmaceutical Assessor)
Mr J Grimshaw (Secretary)
Mr K L Fowler
Mr T J Kirkley
Dr P N Adams
Mr A C Cartwright
Miss R Coulson
Dr M Duncan
Dr S Fawcett
Dr L K Fowler
Dr A J Isaacs
Dr W J Jenkins
Mrs S Kelly
Dr A Nath
Dr J C Ritchie
Mr A G Stewart
Dr C Twomey
Dr K Winship
Dr S Wood

Also Present

Mr C Davies
Mr D Hagger
Mr N Hale
Dr H Pickles

1. Apologies and Announcements

1.1 The Chairman repeated his usual reminder that the papers and proceedings are confidential and should not be disclosed.

1.2 Apologies for absence had been received from Mr Darling, Professor Jacobs and Dr Castleden.

1.3 The Chairman introduced and welcomed Professor McGee, a member of the SEAR Sub-Committee, and Dr Bangham from NIBSC.

2. Minutes of the Meeting held on 25 October 1984

After some typographical errors had been corrected the Chairman signed the minutes as a true record of the meeting.

3. Matters arising from the Minutes

Paper 5 Actifed Syrup

Professor Asscher reported that CRM had recently discussed adverse reactions in children arising from use of the related product, phenylpropanolamine (PPA). It was uncertain if children were more susceptible to PPA or whether reactions were more frequently reported in children because of relative overdosing. This aspect could be considered when the Current Problems article on Actifed is being written.

4. Consideration of Applications

4.1 The Committee considered the applications listed and their advice is given in Annex A.

4.2 Vermox Tablets : PL/0242/0011 : Janssen Pharmaceuticals.

4.2.1 The Committee deferred consideration of this application so that it could be referred back to the SEAR Sub-Committee for re-evaluation of the toxicity data in children under 2 years of age, and to consider why it is not recommended for that age group. The Committee also asked the SEAR Sub-Committee to give further consideration to the recommendation for pharmacy sale of other teratogenic anthelmintics with a view to preparing an item for inclusion which should be included in a future issue of Current Problems.

4.2.2 Professor Grahame-Smith declared a non-specific interest.

4.3 Lasma SR : PL/0108/0084-5 : Pharmax Ltd
Microphyllin Microcaps : PL/0339/0015-17 : Radiol Chemicals
Somophyllin CRT Capsules 350mg : PL/0113/0107 : Fisons PLC
Provent Capsules : PL/0003/0206 : Wellcome Foundation

The Committee deferred consideration of these applications until a paper on the Bioavailability of Oral Sustained Release Theophyllin Preparations, itself deferred from the October Meeting of CSM, was available.

4.4 Nizatidine Capsules : CT/0006/0187 : Lilly Industries

Professor Elworthy declared a non-specific interest.

4.5 Pergolide Mesylate Capsules : CT/0006/0190 : Lilly Industries

Professor Elworthy declared a non-specific interest.

4.6 Velosulin 100 i.u./ml cartridge vials : PL/3132/0043 : Nordisk (UK) Ltd

In connection with this application the Committee asked to be informed of the outcome of the evaluation of the safety of the Nordisk pump.

5. Hearing

5.1 The Committee held a hearing on the following:

Pulmicort Inhaler : PL 0017/0128	)
Pulmicort Paediatric Inhaler : PL 0017/0113	)
Rhinocort Nasal Aerosol : PL 0017/0204	)
Preferid Ointment : PL 0017/0097	) Astra Pharmaceuticals
Preferid Cream : PL 0017/0102	)
Pulmicort Aerosol : CTC 0017/0091	)

5.2 The Committee's advice and reasons for that advice are given in Annex B.

6. Paper 1 - Arbaprostil

6.1 The Committee considered this paper and the recommendation of the SEAR Sub-Committee.

6.2 The Committee endorsed the Sub-Committee recommendation that:

6.2.1 Clinical Trials for Arbaprostil should be allowed to proceed providing the present protocol (200 g/day for 7 days) is strictly adhered to.

6.2.2 The full results of the carcinogenicity studies in two species should be submitted with any application to extend the treatment period or to treat at higher doses.

7. Paper 2 - Carcinogenicity of Dibenyline (Phenoxybenzamine)

Dibenyline Capsules : PL/0002/5009 : Smith, Kline & French
Dibenyline Injection Concentrate : PL/0002/5048 : Smith, Kline & French

The Committee deferred consideration of this paper to enable SEAR to re-evaluate efficacy in the management of urinary retention due to neurogenic bladder or prostatic hypertrophy.

8. Paper 3 - Triamterene

8.1 The Committee considered this paper and the recommendation of the SEAR Sub-Committee.

8.2 The Committee endorsed the Sub-Committee recommendation that:

8.2.1 No further action is required at present.

8.2.2 The position should be reviewed when the full results of the carcinogenicity studies are available.

9. Paper 4 - Lendormin Carcinogenicity Studies (PL/0015/0092-93)

9.1 The Committee considered this paper and the recommendation of the SEAR Sub-Committee.

9.2 The Committee endorsed a Licensing Authority proposal that the product licences for Lendormin Tablets containing 0.125mg Brotizolan (PL/0015/0092) and Lendormin Tablets containing 0.250mg Brotizolam (PL/0015/0093) should be revoked on the grounds specified in Section 28(3)(g) of the Medicines Act 1968, namely that they could no longer be regarded as products which could be safely administered for the purposes stated in the licences.

9.3 The reasons for this provisional conclusion were:

9.3.1 There is concern regarding the possible carcinogenic risks associated with the use of these products.

9.3.2 There are no overriding clinical benefits to outweigh these risks.

10. Paper 5 - Potassium Canrenoate, Spironolactone and Oncogenicity

10.1 The Committee considered this paper and the recommendation of the SEAR Sub-Committee.

10.2 The Committee endorsed a Licensing Authority proposal that the product licence for Spirocta∩-M Injection (PL/0075/0040) should be varied under Section 28 of the Medicines Act 1968, on the ground specified in Section 28(3)(g), namely that this product can no longer be regarded as one which can be safely administered for the purposes indicated in the licence, so as to add the wording specified in paragraph 10.3 below to the warnings section of the Schedule of this licence.

10.3 Any data sheet which is issued in respect of the product to which this licence relates shall contain a warning to indicate that chronic oral potassium canrenoate administration causes myelocytic leukaemia in the rat.

10.4 The reason for this provisional conclusion was that there is concern regarding the possible carcinogenic risk associated with the use of Spirocta∩.

10.5 The Committee also endorsed a Licensing Authority proposal that the product licences for products containing Spironolactone (see Annex C) should be varied under Section 28 of the Medicines Act 1968, on the ground specified in Section 28(3)(g), namely that these products can no longer be regarded as products which can safely be administered for the purposes indicated in the licences, so as to restrict the indications of these products to those listed below:

1. Cirrhosis with ascites and oedema.

2. Malignant ascites.

3. Nephrotic syndrome.

4. Diagnosis and treatment of primary hyperaldosteronism.

5. Congestive cardiac failure.

and where this removes all the existing indications, also to revoke the licence.

10.6 The reason for this provisional conclusion was that there is concern regarding the possible carcinogenic risk associated with the long term use of Spironolactone.

10.7 The Committee endorsed the Sub-Committee recommendation that:

10.7.1 The amendment to the data sheet for products containing Spironolactone about potassium canrenoate and myelocytic leukaemia in rats proposed by Searle should be accepted, except that the last sentence of paragraph 1 and the third sentence of paragraph 2 should be deleted, as there is inadequate evidence to substantiate their claims.

10.7.2 Searle should be asked to perform new adequate oral carcinogenicity studies of spironolactone in rats to determine whether it causes myelocytic leukaemia and lymphatic leukaemia.

11. Paper 6 - Guidelines on Control Tests for Synthetic Peptides

11.1 The Committee noted this paper and the comments of the Sub-committees.

11.2 The Committee agreed that, after removal of Appendices A and C and after combining this paper with a paper on the physico-chemical aspects on control of synthetic peptides, the combined paper should be referred to the British Pharmacopoeia Commission for their comments. The Committee considered that the paper should then be submitted to the ABPI for consultation before an entry is made in Current Problems.

12. Paper 7 - Tagamet Tablets 800mg

12.1 The Committee endorsed a Licensing Authority proposal that the product licence for Tagamet Tablets 800mg (PL/0002/0128) should be varied under Section 28(3)(g) of the Medicines Act 1968, so as to add the wording specified in paragraph 12.2 below to the warnings section of schedules to the licence.

12.2 Any data sheet which is issued in respect of the product to which this licence relates shall contain warnings to indicate that gynaecomastia has been reported and this is usually, but not always, reversible on the discontinuation of therapy, and that the following adverse reactions have also been associated with cimetidine therapy, impotence, headache, alopecia, myalgia and arthralgia.

12.3 The reason for this provisional conclusion was that there is concern regarding reports of the adverse reaction to which reference is made in paragraph 12.2 above.

13. Paper 8 - Appointment of a new member to the Sub-Committee on Biological Products (Tabled Paper)

The Committee approved the appointment of Professor E R Moxon to the Sub-Committee on Biological Products. They noted that Professor Moxon

would be invited to attend the Sub-Committee only when there was an application being considered within his speciality.

14. Paper 9 - Committee Papers - Previous Application Papers

The Committee were unable to accept the Secretariat's proposal that previous papers should no longer be circulated as part of current papers.

15. Written Representation

15.1 The Committee considered a written representation on the following product:

Berofor Nasal Spray : CT/0015/0101 : Boehringer Ingelheim.

1.52 The Committee's advice and reasons for that advice are given in Annex D.

16. Secretary/Medical Assessor's Oral Report

None.

17. Any Other Business - AIDS

Dr J Smith informed the Committee that heat treatment of Factor VIII, which is used in the treatment of haemophiliacs, abolished detectable infectivity of AIDS virus added to the preparation. (Source MMWR 1984; 33 N° 42). Therefore, companies should be encouraged to apply for variations of licences to permit widespread use of heat-treated Factor VIII, so that the incidence of AIDS in haemophiliacs might be reduced.

Professor Rawlins reminded the Committee that heat-treated Factor VIII is more expensive than the standard preparation. Widespread substitution of the heat-treated product may cause haemophilia centres to exceed their budgets.

The Committee requested that the Licensing Authority propose to the Companies concerned that they make early applications for variations to use a dry heat treating process in the manufacture of their Factor VIII products.

18. Date and Time of Next Meeting

Thursday 20 December 1984 at 10.30 am.