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CSM/82/2nd Meeting

NOT FOR PUBLICATION

COMMITTEE ON SAFETY OF MEDICINES

Minutes of the Meeting held on Thursday 25 February 1982

Present

Professor A Goldberg (Chairman)
Professor R H Girdwood
Dr J Holt
Professor A E A Read
Professor H K Weinbren
Professor M Rawlins
Dr J Smith
Professor W I Cranston
Professor D G Grahame-Smith
Professor P H Elworthy
Professor B M Hibbard
Dr M Richards
Professor D Hull
Mr W Darling
Professor H Keen*
Professor F A Jenner

Committee Secretariat

Dr G Jones (Medical Assessor)
Dr J Calderwood (Pharmaceutical Assesor)
Miss Z Spencer (Secretary)
Dr C Speirs
Dr J Dobbs
Dr S Grieve
Dr K Fowler
Dr R Corcoran
Dr W Ashton
Mr A C Cartwright
Dr Twomey
Dr L Hill
Dr G Diggle
Dr G Venning
Mr J S Bird
Dr A Nath
Dr A Andrews
Dr P Weber
Mrs J Archer
Mrs K Sherrington
Mrs G Harrison
Mr A Ramsingh

Also Present

Mr N Williams
Dr W Thomas
Mr P Allen
Mr R Butcher
Mr P Morris
Dr A T B Moir

*Present for Hearing 1 only.

1. Apologies and Announcements

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

1.2. On behalf of the Committee the Chairman welcomed

a. Professor Hull who was attending his first meeting as a member of the Committee.

b. Professor Keen who had been appointed as a member of the Committee for the day for the hearing on Atromid-S (clofibrate).

c. Dr Dobbs who was attending his first meeting since joining the Medical Secretariat as a Senior Medical Officer.

1.3. The Chairman informed members that Dr Venning was attending his last meeting of the Committee prior to taking up a post in the industry. On behalf of the Committee the Chairman thanked him for the contribution he had made to the work of the Committee and wished him every success for the future.

1.4. Apologies for absence were received from Professor Vessey, Professor Dundee, Professor Crooks and Dr Fish.

2. Minutes of the meeting held on 21 January 1982

The minutes were agreed and signed by the Chairman as a correct record.

3. Matters arising from the minutes

There were none.

4. Consideration of Applications

The Committee considered those applications listed. Details of their advice are at Annex A to these minutes.

5. Debendox: Paper 3

5.1. This paper sought the Committee's advice on the significance of two animal teratogenicity studies and an application to vary the product licence of right. The two studies were of doxylamine Succinate/ Bendectin in rats and mice, and crab-eating macaque monkeys respectively. The SEAR Sub-Committee at its meeting on 12 February 1982 had recommended that expert opinions should be sought. It had been possible in the interval since SEAR met to obtain the advice of Professor Poswillo and this was reported verbally by Dr Weber.

5.2. Professor Poswillo considered that no conclusions could be drawn from the studies. In the monkey study, the foetus had probably been sacrificed too early, so that heart development was not complete. The rat and mouse study gave insufficient information; in particular the question of distribution of diaphragmatic hernia between litters, and whether there were sub-mucocutaneous cleft palates. In the light of this advice it was agreed that these studies did not give cause for concern and the Committee saw no reason to alter their previous advice, namely that there was no scientifically acceptable evidence that Debendox caused harm to the foetus. As a precaution it was agreed that the views of one more outside expert should be sought and it was agreed that copies of the studies should be sent to Professor Sullivan.

5.3. On the application for variation the Committee endorsed the recommendation of SEAR that consideration of the application should be deferred, and that the company should be asked to provide the full report of the 8-way efficacy study which led to the removal of dicyclomine hydrochloride from the US formulation. The Committee agreedthat this study should be examined initially by Professor Rawlins, Professor Hibbard and Dr Sutherland with a view to assessing the efficacy of the 2-ingredient formulation in relation to the existing product. In the event that this assessment raised doubts about the comparative efficacy of the two ingredient formulation, the matter would be referred back to SEAR.

6. Mianserin and Arthritis/Arthralgia: Paper 2

6.1. Professor Grahame-Smith introduced this paper which described a hitherto unsuspected association between the administration of mianserin and the incidence of arthritis/arthralgia.

6.2. After discussion it was agreed that the recommendation of the SEAR Sub-Committee should be endorsed and that

a. the company should be approached informally to include these reactions in the warnings section of the data sheet

b. an item on the subject should be included in Current Problems No 8

c. a copy of C.P No 8 should be drawn to the attention of the Research Committee of the Royal College of Psychiatrists, the Evaluation and Research Advisory Committee of the British Association for Rheumatology and Rehabilitation and the Royal College of General Practitioners.

6.3. It was noted that Mianserin was currently being considered by the CRM and that the Secretariat would co-ordinate any action with the Secretariat of that Committee.

7. Hearings

7.1. The Committee held two hearings in respect of

a. Atromid-S (clofibrate): ICI PLR 0029/5022

b. Rowachol: Rowa Limited: PL 0007/0002

7.2. Details of the Committee's advice and the reasons for that advice are at Appendices B and C respectively.

8. Written Representations

8.1. The Committee considered five written representations in respect of

a. Etodoloc: CT 0607/0044

b. Gammabulin: PL 0215/0018-0019

c. H-B-Vax: PL 0025/0165

d. Condranol: CT 4471/0001

e. Meruvax II: PL 0025/0144

8.2. Details of the Committee's advice are at Appendices D-H respectively.

9. Ferridex 50 : A/S Rosco : Suspension of Product Licence Paper 1

The Committee noted the further suspension of this licence for a period of 3 months from 27 January 1982.

10. Secretary and Medical Assessors Oral Report

None.

11. Items for Information

11.1. CSM/ABPI Annual Dinner Meeting

The Chairman informed members that later that day representatives of the Committee together with members of the Secretariat would be meeting the ABPI. Members had before them a paper which detailed some of the subjects which were likely to be discussed.

11.2. Minutes of SEAR 8 January 1982

Professor Grahame-Smith drew the attention of members to the concern expressed by the SEAR Sub-Committee regarding the increasing backlog of uncoded yellow card adverse reactions reports. The CSM showed this concern.

11.3. Minutes of Adverse Reactions 8 October 1981

Professor Cranston informed the Committee that his investigations regarding X-Prep and Colonic Perforation were continuing and that a paper would be prepared on the subject in due course.

12. Any other business

There was none.

13. Date and Time of Next Meeting

Thursday 25 March 1982 at 10.30am.

Re. PL 2777/0003

CTX.

Biotest Polex Ltd.

Product

Dried Seralo VIII Antihaemophilic Factor (Human)

Therapeutic Class

Blood product

Active Constituent

Antihaemophilic factor (Factor VIII) Concentrate from frozen human plasma

Main Committee 25.2.82

Advice

On the evidence before them the Committee had reason to think that on grounds relating to quality and safety in relation to quality, they would be unable to advise the grant of a product licence for this preparation and directed the Secretary to notify the applicant in accordance with Section 21(1) of the Act.

The Committee provisionally concluded that:

1. further information should be provided on the source and collection of plasma

2. further information on the manufacture and control of manufacture should be provided

3. formal finished product specifications should be provided for each of the four proposed strengths of this product, and the product(s) should satisfy the criteria of the Ph Eur tests for abnormal toxicity, pyrogenicity and sterility

4. the stability data presented was inadequate

5. information presented on the batch analysis of one lot as evidence of consistency of manufacture was inadequate.

Remarks

1. Labels should comply with the Medicines (Labelling) Regulations (1976) and data sheets should comply with the Medicines (Data Sheet) Regulations (1972) and subsequent amendments.

2. The name of the qualified person responsible for the product in the UK should be provided.

3. Samples and protocols should be supplied to the NIBSC.

No. PL 2777/0004

Coy.

Octest Polex Ltd.

Product

ormal Serum Albumin (Human)

Therapeutic Class

lood Product

Active Constituent

lbumin prepared from ooled normal venous lasma (human)

Main Committee

25.2.82

Advice

On the evidence before them the Committee had reason to think that on grounds relating to quality and safety in relation to quality were unable to advise the grant of a product licence for this preparation and directed the Secretary to notify the applicant in accordance with Section 21(1) of the Act.

The Committee provisionally concluded that:

1. clear statements should be made regarding the products - strength, container size and proposed indication for which licences are being sought.

2. further information should be given on the source and collection of plasma

3. further information on the manufacture and control of manufacture should be given

4. formal specifications should be provided for the bulk freeze dried material and for each of the finished dosage forms, and the products should satisfy the criteria of the Ph Eur tests for abnormal toxicity, pyrogenicity and sterility, when tested

5. the stability data presented was inadequate

6. further evidence should be given on the consistency of manufacture, in the form of batch analyses

7. information should be provided on Pre-Kallikrein Activator levels of batches for this product.

Remark

1. Labels should comply with the Medicines (Labelling) Regulations (1976) and data sheets should comply with the Medicines (Data Sheet) Regulations (1972) and subsequent amendments.

2. The name of the qualified person responsible for the product in the UK, along with details of the tests to be undertaken on the product on importation should be provided.

3. Samples and protocols should be supplied to the NIBSC.

No. PL 3132/0022-25

Coy.
Nordisk - UK limited

Product
Factor VIII Nordisk 250, 350, 500, 700 IU.

Therapeutic Class
Blood Product

Active Constituent
Human Coagulation Factor VIII 250/350/500/700 IU

Main Committee 25.2.82

Advice

On the evidence before them the Committee had reason to think that on grounds relating to quality and efficacy, they were unable to advise the grant of a product licence for this preparation and directed the Secretary to notify the applicant in accordance with Section 21(1) of the Act.

The Committee provisionally concluded that:

1. inadequate evidence was provided to justify the claim that the product degraded more slowly than conventional Factor VIII preparations

2. further information should be provided on the controls exerted over plasma collection

3. further information should be provided on the manufacturing process

4. further information should be provided on the quality control of batches and sub-batches

5. further information should be provided on the stability of the product.

Remarks

1. A satisfactory inspectors report would need to be obtained to verify the plasma sources prior to the grant of a product licence.

2. In the event of a product licence being granted batch release procedures would be required.

3. Samples and protocols should be supplied to the NIBSC.