APPENDIX 'A'

COMMITTEE ON SAFETY OF MEDICINES

Appendix A to minutes of meeting held on 22 February 1973

Summary of recommendations and advice on applications

CT/0004/0223

Glaxo Laboratories Ltd

Betnovate Aerosol
(Nasal Decongestant)

Sub-Committee on Toxicity and Clinical Trials

On the evidence before them the Sub-Committee recommend the issue of a clinical trial certificate for this preparation for the purposes indicated in the application, provided that:

(i) children under 12 are excluded from the studies.

(ii) treatment is not continued for longer than 3 weeks

(iii) blood cortisol estimations or corticotrophin stimulation tests are carried out on each patient at 0, 1 and 3 weeks.

Remarks

Before an extension of the trials can be agreed the initial results should be submitted for consideration.

Main Committee

On the evidence before them the Committee advise the issue of a clinical trial certificate for this preparation for the purposes indicated in the application, provided that:

(i) children under 12 are excluded from the studies.

(ii) treatment is not continued for longer than 3 weeks

(iii) blood cortisol estimations are carried out on each patient at 0, 1 and 3 weeks.

CT/0012/0080

May & Baker Ltd

19,583 RP Capsules

(Non-steroidal Anti-inflammatory)

Sub-Committee on Toxicity and Clinical Trials

On the evidence before them the Sub-Committee recommend that the clinical trials of this preparation be extended to include women of child-bearing age, provided that they are advised to avoid becoming pregnant, and provided that careful monitoring for gastro-intestinal bleeding is undertaken.

The Sub-Committee further recommend that pregnant women should still be excluded from the trials.

Main Committee

On the evidence before them the Committee advise that the clinical trials of this preparation be extended to include women of child-bearing age, provided that they are advised to avoid becoming pregnant, and provided that careful monitoring for gastro-intestinal bleeding is undertaken.

The Committee further recommend that pregnant women should still be excluded from the trials.

CT/0012/0085

May & Baker Ltd

M & B 18,706 Capsules

(Phenothiazine Antispasmodic Agent)

Sub-Committee on Toxicity and Clinical Trials

On the evidence before them the Sub-Committee recommend that the clinical trials of this preparation be extended as requested in the application, including administration to women of child-bearing age, provided that:

(i) they are advised to avoid becoming pregnant

(ii) pregnant women are excluded from the trials.

Main Committee

On the evidence before them the Committee advise that the clinical trials of this preparation be extended as requested in the application, including administration to women of child-bearing age, provided that:

(i) they are advised to avoid becoming pregnant

(ii) pregnant women are excluded from the trials.

CT/0018/0037

Parke, Davis & Co

CI-583 Na Capsules

(Anti-inflammatory)

Sub-Committee on Toxicity and Clinical Trials

On the evidence before them the Sub-Committee recommend the issue of a clinical trial certificate, provided that the trial is initially limited to a study of 30 in-patients at one centre only, for a period of up to 4 weeks treatment, with monitoring of renal function and blood loss.

Remarks

Before consideration could be given to an extension of the trial the results of all studies in progress in animals and man would be required.

Main Committee

Subject to the Sub-Committee on Chemistry and Pharmacy being satisfied and on the evidence before them the Committee advise the issue of a clinical trial certificate, provided that the trial is initially limited to a study of 30 in-patients at one centre only, for a period of up to 4 weeks treatment, with monitoring of blood loss and possible nephrotoxicity.

CT/0286/0041

Syntex Pharmaceuticals Ltd

The QOD Pill

(Oral Contraceptive)

Sub-Committee on Toxicity and Clinical Trials

On the evidence before them the Sub-Committee recommend the issue of a clinical trial certificate for this preparation for the purposes indicated in the application.

Main Committee

On the evidence before them the Committee advise the issue of a clinical trial certificate for this preparation for the purposes indicated in the application.

CT/0286/0042

Syntex Pharmaceuticals Ltd

Anapolon 5 Tablets

(Anabolic Steroid)

Sub-Committee on Toxicity and Clinical Trials

On the evidence before them the Sub-Committee are unable to recommend the issue of a clinical trial certificate for this preparation for the purposes indicated in the application because of its carcinogenic potential and hepatotoxicity.

Main Committee

On the evidence before them the Committee concluded provisionally that on the ground of safety they would be unable to advise the issue of a clinical trial certificate for this preparation for the purposes indicated in the application because of its lack of safety with regard to liver damage.

Accordingly it was agreed that action under Section 21(1) of the Medicines Act would be required.

CT/0512/0028

Duphar Laboratories Ltd

DU 34,796 Capsules

(Antiviral Agent)

Sub-Committee on Biologicals (January 1973)

On the evidence before them the Sub-Committee on Biologicals have no objection to the issue of a clinical trial certificate for this preparation for the purposes indicated in the application.

Sub-Committee on Toxicity and Clinical Trials (February 1973)

On the evidence before them the Sub-Committee recommend the issue of a clinical trial certificate for this preparation for the purposes indicated in the application.

Remarks

The applicant's attention should be drawn to the possibility of CNS stimulation and the possible hazard of dependence.

Main Committee (February 1973)

Subject to the Sub-Committee on Chemistry and Pharmacy being satisfied and on the evidence before them the Committee advise the issue of a clinical trial certificate for this preparation for the purposes indicated in the application.

PL/0015/0044
PL/0015/0045

Boehringer Ingelheim Ltd

Tranxene Capsules 7.5 mg.
Tranxene Capsules 3.5 mg.

(Anxiolytic)

Sub-Committee on Toxicity and Clinical Trials

Recommendation

On the evidence before them the Sub-Committee recommend the grant of product licences for these preparations for the purposes indicated in the application.

Main Committee

Subject to the Sub-Committee on Chemistry and Pharmacy being satisfied and on the evidence before them the Committee advise the grant of product licences for these preparations for the purposes indicated in the application.

The Committee also advise that these products should be regarded as new for the purpose of a special directive for the reporting of adverse reactions.

PL/0086/0021
PL/0086/0022

Hoechst Pharmaceuticals

BL 191 Tablets
BL 191 Injection

(Vasodilator)

Sub-Committee on Toxicity and Clinical Trials (January 1973)

The Sub-Committee recommend that a decision on these products should be deferred for consideration of additional data which has been submitted and clarification of indications.

Main Committee (January 1973)

The Committee agree that a decision on these products should be deferred pending:

(i) consideration of additional data which has been submitted

(ii) clarification of the indications

(iii) receipt of the views of the Sub-Committee on Chemistry and Pharmacy.

Sub-Committee on Toxicity and Clinical Trials (February 1973)

On the evidence before them the Sub -Committee recommend the grant of product licences for these preparations for the purposes indicated in the application, provided that the claims are limited to peripheral vascular disease only.

Remarks

The other indications are rejected on the grounds of inadequate evidence of efficacy.

Main Committeee (February 1973)

Subject to the Sub-Committee on Chemistry and Pharmacy being satisfied and on the evidence before them the Committee advise the grant of product licences for these preparations for the purposes indicated in the application, provided that the claims are limited to peripheral vascular disease only. The Committee agree that the other indications should be rejected on the ground of inadequate evidence of efficacy.

The Committee also advise that these products should be regarded as new for the purposes of a special directive for the reporting of adverse reactions.

PL/0095/0010

Cyanamid of Great Britain Ltd

Parfenac Cream

(Anti-inflammatory Cream)

Sub-Committee on Toxicity and Clinical Trials
(December 1972)

On the evidence before them the Sub-Committee are unable to recommend the grant of a product licence for this preparation for the purposes indicated in the application, since there is inadequate evidence of efficacy for the proposed indications, associated with possible toxicity.

Main Committee (December 1972)

The Committee decided to refer this application back to the Sub-Committee on Toxicity for review of the evidence on efficacy, in particular with regard to additional information on toxicity if it can be obtained.

Sub-Committee on Toxicity and Clinical Trials
(February 1973)

On the evidence before them the Sub-Committee recommend the grant of a product licence for this preparation for the purposes indicated in the application.

Main Committee (February 1973)

Subject to the Sub-Committee on Chemistry and Pharmacy being satisfied and on the evidence before them the Committee advise the grant of a product licence for this preparation for the purposes indicated in the application.

The Committee also advise that this product should be regarded as new for the purpose of a special directive for the reporting of adverse reactions.

PL/0132/0025
PL/0132/0026

Wander Limited

AN 448 Tablets 1 mg.
AN 448 Tablets 2 mg.

(Anorectic Agent)

Sub-Committee on Toxicity and Clinical Trials

The Sub-Committee recommend that a decision on these products should be deferred pending receipt of:

(i) information on what is being absorbed, metabolism and interaction with anti-hypertensive drugs and catechol amines.

(ii) information on the possible effects of the drug on brain seratonin stores and the possible relationship to mood changes in man

(iii) an explanation for the high drop-out level in the clinical trial.

Main Committee

The Committee agree that a decision on these products should be deferred pending receipt of:

(i) information on what is being absorbed, metabolism, and interaction with anti-hypertensive drugs and catechol amines

(ii) information on the possible effects of the drug on brain seratonin stores and the possible relationship to mood changes in man

(iii) an explanation for the high drop-out level in the clinical trial

(iv) the views of the Sub-Committee on Chemistry and Pharmacy

PL/0161/0012

Rona Laboratories Ltd

Madecassol Tablets

(Wound Healing Agent)

Sub-Committee on Toxicity and Clinical Trials (January 1973)

On the evidence before them the Sub-Committee recommend the grant of a product licence for this preparation provided that the indications are limited to defective scars and keloids.

Remarks

Before consideration could be given to an extension to include the other proposed indications, adequately controlled clinical studies would be required.

Main Committee (January 1973)

On the evidence before them the Committee decided to refer this application back to the Sub-Committee on Toxicity and Clinical Trials to review their recommendation in the light of the views of the Sub-Committee on Chemistry and Pharmacy, in particular on the question of definition of the active constituents.

Sub-Committee on Toxicity and Clinical Trials (February 1973)

On the evidence before them the Sub-Committee are unable to recommend the grant of a product licence for this preparation for the purposes indicated in the application due to inadequate evidence of efficacy.

Remarks

The Sub-Committee would have no objection to an adequately controlled clinical trial being undertaken.

Main Committee

On the evidence before them the Committee concluded provisionally that on the ground of efficacy they would be unable to advise the grant of a product licence for this preparation for the purposes indicated in the application due to inadequate evidence of efficacy.

Accordingly it was agreed that action uder Section 21(1) of the Medicines Act would be required in the course of which account should be taken that the views of the Sub-Committee on Chemistry and Pharmacy had yet to be received.

NOTE

The Committee agreed that subject to the Sub-Committee on Chemistry and Pharmacy being satisfied, no objection would be raised to an adequately controlled clinical trial being undertaken and that a certificate might be issued without further reference to the Committee.

PL/0215/0003

Serological Products Ltd

Kryobulin

(Blood Product)

Sub-Committee on Biologicals (January 1973)

On the evidence before them the Sub-Committee on Biologicals recommend the grant of a product licence for this preparation for the purposes indicated in the application, provided that:

(i) the potency of the product is expressed in international units

(ii) the supply of the product is restricted to hospitals and haemophilia centres

(iii) the TSA batch release procedure shall apply.

Sub-Committee on Toxicity and Clinical Trials (February 1973)

On the evidence before them the Sub-Committee recommend the grant of a product licence for this preparation for the purposes indicated in the application.

Main Committee (February 1973)

On the evidence before them the Committee advise the grant of a product licence for this preparation for the purposes indicated in the application, provided that:

(i) the potency of the product is expressed in international units.

(ii) the supply of the product is restricted to hospitals and haemophilia centres

(iii) the TSA batch release procedure shall apply.

The Committee also advise that this product should be regarded as new for the purpose of a special directive for the reporting of adverse reactions.

PL/0247/0007

Burton, Parsons & Co Inc

Adsorbotear TM (Adapt)

(Ophthalmic Preparation)

Sub-Committee on Toxicity and Clinical Trials

The Sub-Committee recommend that a decision on the product should be deferred pending receipt of expert opinions from three ophthalmologists.

Remarks

Provided that the views of the ophthalmologists are favourable the issue of a clinical trial certificate could be recommended, but further data would be required before granting a product licence.

Main Committee

The Committee agree that a decision on this product should be deferred pending receipt of expert opinions from three ophthalmologists. The Committee also agree that provided the views of the ophthalmologists are favourable the issue of a clinical trial certificate could be recommended, but furthur data would be rquired before granting a product licence.

PL/0432/0002

Kemsales Limited

Besorbon Medicinal Snuff

(Nasal Decongestant)

Sub-Committee on Toxicity and Clinical Trials

The Sub-Committee recommend that a decision on this product should be deferred pending receipt of evidence of safety and efficacy.
Evidence that the preparation does not cause local irritation would be required.

Main Committee

The Committee agree that a decision on this product should be deferred pending receipt of evidence of safety and efficacy, including evidence that the preparation does not cause local irritation.

PL/0632/0001

Himalaya Drug Co Private Limited

Cystone Tablets

Sub-Committee on Toxicity and Clinical Trials

On the evidence before them the Sub-Committee are unable to recommend the grant of a product licence for this preparation for the purposes indicated in the application due to inadequate evidence of safety and efficacy.

Main Committee

On the evidence before them the Committee concluded provisionally that on the grounds of safety, quality and efficacy they would be unable to advise the grant of a product licence for this preparation for the purposes indicated in the application due to:

inadequate evidence of quality, safety and efficacy because of insufficient information on:-

(a) the botanical and mineral sources of the "active constituents"

(b) the processes of manufacture of the extracts; the nature, quality and stability of the extracts, or the presence within them of any identifiable component of proven pharmacological or therapeutic activity.

(c) toxicity studies and clinical evidence.

Accordingly it was agreed that action under Section 21(1) of the Medicines Act would be required.

PL/1752/0005

Nicholas Laboratories Ltd

Feximac Cream

(Anti-inflammatory Cream)

Sub-Committee on Toxicity and Clinical Trials (December 1972)

On the evidence before them the Sub-Committee are unable to recommend the grant of a product licence for this preparation, since there is inadequate evidence of efficacy for the proposed indications, associated with possible toxicity.

Main Committee (December 1972)

The Committee decided to refer this application back to the Sub-Committee on Toxicity for review (in conjunction with application PL/0095/0010) of the evidence on efficacy in particular with regard to additional information on toxicity if it can be obtained.

Sub-Committee on Toxicity and Clinical Trials (February 1973)

On the evidence before them the Sub-Committee recommend the grant of a product licence for this preparation for the purposes indicated in the application. .

Main Committee (February 1973)

Subject to the Sub-Committee on Chemistry and Pharmacy being satisfied and on the evidence before them the Committee advise the grant of a product licence for this preparation for the purposes indicated in the application.

The Committee also advise that this product should be regarded as new for the purpose of a special directive for the reporting of adverse reactions.

PL(R)/0286/5009

Syntex Pharmaceuticals Ltd

Anapolon 50 Tablets

(Anabolic Steroid)

Sub-Committee on Toxicity and Clinical Trials

On the evidence before them the Sub-Committee recommend that the product licence of right be extended to include the indication for use as an adjuvant to therapy in patients with malignant disease where treatment with cytotoxic agents or radiotherapy is likely to cause bone marrow depression.

Remarks

A decision relating to use in patients with renal failure should be deferred for further evidence of efficacy.

Main Committee

On the evidence before them the Committee advise that the product licence of right be extended to include the indication for use as an adjuvant to therapy in patients with malignant disease where treatment with cytotoxic agents or radiotherapy is likely to cause bone marrow depression.

The Committee agree that a decision relating to use in patients with renal failure should be deferred for further evidence of efficacy.