MINUTES OF THE SEVENTEENTH MEETING OF THE MEDICINES CLASSIFICATION COMMITTEE HELD IN THE THERAPEUTICS SECTION OF THE MINISTRY OF HEALTH ON THE EIGHTEENTH FLOOR OF GRAND PLIMMER TOWERS, 4-6 GILMER TERRACE, WELLINGTON ON THURSDAY 15 MAY 1997 COMMENCING AT 9:30AM

PRESENT

Dr Bob Boyd (Chair)
Dr Stewart Jessamine
Dr Tim Bevin
Mr David Thompson
Mr Bernard McKone

Mrs Carol Smith (Secretary)

1 WELCOME

Dr Boyd opened the meeting at 9:30am and welcomed committee members to their new positions. He asked if all members had received a copy of the Members' Handbook and enquired about why it was referred to as a draft. The Secretary explained that the Therapeutics Section was currently reviewing the way in which the consultation process was undertaken and it was this section of the Handbook which was under review.

Dr Boyd spent a few moments explaining the legislation relating to the Medicines Classification Committee including the consultation required as part of the reclassification process. He outlined the way recommendations are implemented as regulations through section 105 of the Medicines Act 1981 and explained how recommendations could also be put into effect on a temporary basis by means of a notice in the *Gazette* under section 106 of the Act. Dr Boyd pointed out that the Ministry could provide parallel advice alongside that of the Committee, especially if it were not in agreement with a particular recommendation or possessed additional policy information on that matter.

2 APOLOGIES

An apology was received from Dr Graham Wardrope.

3 CONFIRMATION OF THE MINUTES OF THE SIXTEENTH MEETING

Dr Boyd explained that the members of the previous committee had signed a declaration accepting the minutes as an accurate record of the sixteenth meeting. It was noted that there had been an amendment made at the request of one of the members and that this amendment had been incorporated into the minutes. As there was no member of the previous committee present to confirm that the minutes were an accurate record of the sixteenth meeting, Dr Boyd said that he would sign them conjointly with the previous chairperson at a later date.

4 DECLARATION OF CONFLICT OF INTERESTS

Members each made an oral declaration of any interests which they felt might lead to a possible conflict of interests. The chairman was unable to identify any issues which would prejudice recommendations made in regard to any of the agenda items to be discussed during the meeting and ruled that there was no need for any member to submit a written declaration.

5 INTRODUCTION TO REGULATORY PROCESSES

Dr Jessamine spoke to a paper he had prepared explaining the regulation medicines in New Zealand and the relationship of classification to other regulatory processes. Copies of the paper were circulated.

Dr Boyd told the committee about how the new draft Therapeutics Products Bill currently being developed would introduce product licensing. This would get rid of the situation with the current legislation where "medicine" meant both a product and an active ingredient.

Some time was spent discussing what constituted a medicine as defined in the Medicines Act. The distinction between medicines and dietary supplements was explored and the significance of therapeutic claims emphasised. A number of currently controversial products were referred to as illustrations.

Before moving on to the business on the agenda, Dr Boyd suggested that members tell the committee a little about their professional backgrounds, skills and areas of special interest. Members each gave a brief outline. It was noted of particular relevance that Dr Bevin was involved in drug and alcohol abuse rehabilitation and that Mr McKone had recently completed the degree of Master of Pharmacy Practice for which his thesis was on smoking cessation and the role that pharmacists can play. Both Mr McKone and Mr Thompson were especially interested in developing and maintaining good standards of pharmacy practice.

6 MATTERS ARISING

(i) Cetirizine and loratadine

At the sixteenth meeting the Committee had requested that the Medicines Adverse Reactions Committee (MARC) should actively seek further information about cetirizine and loratadine. The request followed the recent reclassification of terfenadine and astemizole from pharmacy-only to restricted medicine. The Committee noted that correspondence with the MARC had produced no further data which would cause them to wish to reconsider the present classification of either cetirizine or loratadine.

Dr Boyd tabled a letter to *The Lancet* from the Uppsala Monitoring Centre[1] which suggested that world-wide reports of cardiac irregularities seemed similar for all non-sedating antihistamines and that it might not be right to distinguish between them. In the general discussion which followed it was agreed that there was insufficient information to determine

[1] *The Lancet* volume 349, number 9061 *Risks of non-sedating antihistamines,* WHO Centre for International Drug Monitoring, Uppsala, Sweden.

whether the adverse reactions for all five non-sedating antihistamines was due to the antihistamine alone or to interactive effects with other medicines or to other concurrent medical conditions.

Dr Jessamine told the Committee that the reason the MARC was looking again at terfenadine was not that there were new adverse reactions data about terfenadine but rather that fexofenadine had recently received consent to market. He explained that fexofenadine was a metabolite of terfenadine marketed by the same company. Unlike terfenadine, fexofenadine had been shown not to have the same potential to increase the QT interval. He added that those countries where terfenadine had been further restricted were mainly those where fexofenadine was already being marketed. The restriction of terfenadine was due not to the fact that terfenadine had been shown to be any worse than previously, but that fexofenadine had been shown to be better. Fexofenadine had been given consent in New Zealand but was not expected to be actively marketed until the middle of the year. Until that time there appeared to be little basis for regulatory action to restrict terfenadine further as there was a very low risk factor on which to base a regulatory recommendation.

It was noted that products containing astemizole were those most likely to suffer on the market in that they were more restrictively classified than loratadine, cetirizine or acrivastine, all of which appeared to have a very low rate of interaction with the electrical system of the heart. Unlike terfenadine, there was no metabolite to replace astemizole. Dr Jessamine added that it was the unmetabolised terfenadine and the unmetabolised astemizole which caused the problem with the QT interval.

Recommendation

That no further action was necessary at that point with regard to the classification of loratadine or cetirizine.

(ii) Paracetamol (SmithKline Beecham)

The company had submitted an application to the Committee in April 1996 requesting an increase in the amount of solid dose paracetamol available as a general sale medicine from 10 grams or 20 units per pack to 12.5 grams or 25 units per pack in order to harmonise with Australian classification. The former Committee had recommended no change to the amount of paracetamol available for general sale. The company had subsequently made a new submission.

The Chairman remarked on the fact that not all the Ministry reports were dated or attributed to individuals. Dr Jessamine explained that this was because they were intended to reflect the view of the Section rather than that of an individual. He added that they had all been peer reviewed by discussion at an evaluation review meeting.

Dr Boyd suggested that future evaluator's reports should be signed off by the Section manager. The Committee agreed to this. It was also suggested that, due to the bulk of papers to be reviewed, a colour coding system for the evaluator's reports would be useful. The Secretary agreed to copy the evaluator's reports on coloured paper.

Dr Jessamine explained that the 10 gram pack size limit for general sale had been based on a conscious decision to keep the pack size below the generally accepted adult hepatotoxic dose of 12-15 grams.

An open letter from North Sore Hospital was tabled as evidence of the ease in which multiple numbers of packs were being obtained from supermarkets for suicide attempts.

It was also noted that the rate of self-poisonings from paracetamol was on the increase in Britain and there had been a proposal to reduce the amount of paracetamol available as general sale medicine to a maximum of 12 X 500 milligram tablets or capsules or 6 grams per pack. The Secretary had sought a response from the Medicines Control Agency (MCA) on whether or not this proposal had been implemented. A response had not been received at the time of the discussion.[2]

General discussion of both the company submission and the Ministry report followed. Members did not support an increase in the general sale pack size limits for the reasons outlined in the Ministry report.

Recommendation

That there be no change to the maximum pack sizes of 10 grams or 20 tablets or capsules for solid dose paracetamol available as general sale medicine.

Late agenda item

Paracetamol (Lemsip Flu Strength, Reckitt & Colman)

The Ministry had become aware of a problem with the classification of this product two days before the meeting. It was decided that this item could best be discussed following the other agenda item concerning paracetamol.

The secretary explained to the Committee that in the reconsideration of the classification of all medicines which had taken place in 1990, the Committee had recommended that paracetamol in doses of more than 500 milligrams should be classified as prescription medicine. As there were no products on the market containing more than 500 milligrams per dose unit, this change was not notified in the *Gazette* but was incorporated into the new amendment to the First Schedule of the Medicines Regulations 1984. Consequently the intention for dose units greater than 500 milligrams to be prescription medicines did not come into effect until January 1997 with the publication of Amendment No 7 to the Medicines Regulations. Meanwhile, in 1996, Reckitt and Colman had received consent to market Lemsip Flu Strength, containing 1000 milligrams of paracetamol per sachet, as a pharmacy-only medicine on the basis of the pseudoephedrine content of the product. They had then noticed the prescription medicine entry for paracetamol in the new schedule and had contacted the Ministry urgently to see how the problem could be resolved.

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[2] A response from the MCA was received later in the day and was relayed to the Committee. Implementation of the MCA recommendation had been delayed due to the recent general election.

The Ministry had looked at the labelling of the product and had noted that there was reference on almost every face of the packaging to the fact that the product contained paracetamol. In view of the fact that each sachet contained the equivalent of one adult dose of paracetamol or two 500 milligram tablets, the Ministry did not feel that a prescription classification was appropriate and felt that an adjustment could be made to the medicines schedule to accommodate a powder presentation of paracetamol containing up to 1000 milligrams as a pharmacy-only medicine with a limit of 10 grams per pack.

Dr Jessamine explained the Ministry view to the committee. Members felt comfortable with this. However, they agreed that they would like to see some reference on the pack to this being and adult dose. They agreed that the schedule should be amended to accommodate the product.

Recommendation

That the company be asked to add the words "adult dose form" or similar to the pack.

That pharmacy-only was an appropriate classification for Lemsip Flu Strength.

To accommodate this:

(i) the general sale limit of paracetamol should remain unchanged.

(ii) The prescription medicine entry in the Schedule for paracetamol should be amended to read:

in solid dose form containing more that 500 milligrams per dose unit except when specified elsewhere in this Schedule

(iii) The pharmacy-only entry in the Schedule for paracetamol should be amended to read: in liquid form; in tablet, capsule or powder form containing 500 milligrams or less and in packs containing more than 10 grams; in powder form containing not more than 1000 milligrams per sachet and not more than 10 grams per pack.

Non-Steroidal Anti-Inflammatory Agents

Dr Jessamine spoke to the Ministry report which covered the following four agenda items. Two of these were reapplications for earlier submissions which had been turned down by the previous committee and two were new submissions for a less restrictive classification. Dr Jessamine said that he thought this might be an opportune time to look at the classification of the whole therapeutic group rather than individual medicines within the group. He pointed out that there were several inconsistencies in the classification of some of these, particularly the pharmacy-only classification of mefenamic acid and naproxen sodium for dysmenorrhoea. He suggested that a framework should be established and benchmarks set for each classification category so that all non-steroidal anti-inflammatory medicines could be classified consistently. He added that this proposal might require the reconsideration of the classification of aspirin. It could also mean that the pack sizes of some medicines might need to be considered.

In the general discussion which followed the committee was favourably inclined towards the establishment of a framework to classify all medicines in this group in a consistent manner according to safety profile. It was agreed that appropriate consultation would be necessary with both pharmaceutical companies and specialist bodies. The latter should include such specialists as Dr Richard Robson of the Aspirin Foundation and Dr Tim Maling, chairman of the Medicines Adverse Reactions Committee.

Dr Jessamine agreed to draft a proposed framework for the classification of non-steroidal anti-inflammatories. This document would be completed within 6 weeks of the date of the meeting. It would include details of any classification or other changes which would occur if the framework were to be implemented. Consultation with the above specialists would be undertaken before the draft was sent out to Committee members. The draft would then be sent out to pharmaceutical companies and other interested bodies along with details of any changes to current classifications and comment would be available for discussion at the next meeting of the MCC. In the mean time it was agreed that no changes should be made to the classifications of those medicines which were currently on the agenda. Data which had already been submitted for these medicines would be considered and no further data would be required from companies concerned.

Recommendation

That the Ministry prepare a draft document setting out a framework for the consistent classification of all non-steroidal anti-inflammatory medicines.

That appropriate consultation be undertaken with interested bodies and that the consequences of applying the framework be made clear.

That the matter be placed on the agenda of the next meeting of the MCC.

That no changes be made to the classification of diclofenac, naproxen sodium, ibuprofen or flurbiprofen until a framework had been established for the classification of all non-steroidal anti-inflammatory medicines.

(iii) Diclofenac tablets (Cataflam, Ciba)

A reapplication had been made by the company for the reclassification of 25 milligram tablets in limited pack sizes (30 units) from restricted medicine to pharmacy-only medicine. The Committee had recommended against the change at the April 1996 meeting.

This item was covered in the discussion of non-steroidal anti-inflammatory agents above. The Committee was of the opinion that diclofenac 25 milligram tablets in packs of up to 30 tablets would be likely to be classified as restricted medicine under the proposed framework.

(iv) Naproxen Sodium tablets (Aleve, Roche)

A reapplication had been made by the company for the reclassification of 220 milligram tablets to either pharmacy-only or general sale medicine. The Committee had recommended against the change at the April 1996 meeting.

This item was covered in the discussion of non-steroidal anti-inflammatory agents above. The Committee was of the opinion that, under the proposed framework, a 220 milligram presentation of naproxen sodium would probably be classified as a restricted medicine.

7 SUBMISSIONS FOR RECLASSIFICATION

(i) Ibuprofen tablets (Nurofen Double Strength, Boots)

The company had made a submission for the reclassification from prescription medicine to pharmacy-only medicine of 400 milligram tablets.

This item was covered in the discussion of non-steroidal anti-inflammatory agents above. The Committee was of the opinion that a 400 milligram presentation of ibuprofen would probably be classified as a restricted medicine under the proposed framework

(ii) Flurbiprofen tablets (Froben, Boots)

The company had made a submission for the reclassification from prescription medicine to pharmacy-only medicine of 50 milligram tablets.

This item was covered in the discussion of non-steroidal anti-inflammatory agents above. The Committee was of the opinion that 50 milligram flurbiprofen tablets would probably be classified as restricted medicines under the proposed framework.

(iii) Orphenadrine citrate with paracetamol (Norgesic, 3M)

The company had made a submission for the reclassification from prescription medicine to pharmacy-only medicine of up to 36 tablets each containing 35 milligrams of orphenadrine citrate and 450 milligrams of paracetamol.

Members were concerned about the anticholinergic effects of orphenadrine citrate and potential for abuse of the product. They agreed that there was already a good choice of analgesics available over the counter and that orphenadrine would be more appropriately obtained by prescription.

Recommendation

That there be no change to the current prescription classification of orphenadrine citrate.

(iv) Hydrocortisone in rectal medicines (Proctosedyl Suppositories, Hoechst)

The company had made a submission for reclassification from prescription medicine to restricted medicine of hydrocortisone in rectal suppositories when in combination with cinchocaine. The change would allow suppositories to be classified in the same way as creams and ointments containing the same active ingredients.

The Committee agreed unanimously to this change. Members agreed that a pack limit of 12 suppositories would be appropriate for over-the-counter sale. It was noted that the change would also apply to Xyloproct Suppositories containing hydrocortisone and lignocaine and that the company, Astra, had written in support of this change.

Recommendation

That the Schedule be amended to allow hydrocortisone in combination with a local anaesthetic when in rectal suppositories in pack of not more that 12 suppositories to be reclassified from prescription medicine to restricted medicine.

(v) Nicotine for inhalation (Nicorette Inhaler, Pharmacia Upjohn)

This was a company submission for reclassification from prescription to pharmacy-only medicine. The previous Committee had recommended a prescription medicine classification in May 1995.

Members agreed that there was considerable potential for abuse with this route of administration and felt that a fair amount of counselling and management would be required in order to reduce doses rather than to substitute one addiction with another. They noted that, although very heavy smokers tended to do marginally better on a faster delivery system, this system was not particularly helpful on the behavioural side, with its administration being similar to the act of smoking. One member commented that heavily addicted smokers tended not to get a high enough level of nicotine in the blood early in the day with gum or patches but it was noted that if the correct level of patch was used the blood levels should be sustained over night. The Committee agreed that they would prefer to see this route of administration managed by a medical practitioner until such time as the condition was sufficiently well-managed for the user to be able to move on to patches or gum.

Recommendation

That there be no change to the current classification of inhaled nicotine as a prescription medicine.

(vi) Lithium succinate, topical (Efalith Cream, Scotia)

The Ministry had suggested this as a suitable candidate for reclassification and had received the support of the company for a change from prescription to pharmacy-only medicine.

Members agreed with the Ministry report and were comfortable to recommend that this product become a pharmacy-only medicine. They accepted the Ministry suggestion of 1% of lithium as a cut-off point for topical OTC preparations.

Recommendation

That topical preparations containing 1% or less of lithium be reclassified from prescription medicine to pharmacy-only medicine.

(vii) Azelastine hydrochloride (Rhinolast Nasal Spray, Asta Medica)

This was a company submission for reclassification from prescription to pharmacy-only medicine. The MAAC had earlier recommended a prescription classification and this had been implemented. Azelastine had recently been reclassified as a pharmacy medicine in Great Britain.

The Committee saw a useful place for this as a pharmacy-only medicine as other antihistamine nasal decongestants with this classification were limited to short-term use.

Recommendation

That azelastine for nasal use be reclassified from prescription medicine to pharmacy-only medicine.

(viii) Theophylline Syrup (Nuelin, 3M)

The company had made a submission for reclassification from pharmacy-only to restricted medicine.

The Committee could see no significant safety problem with this medicine and was of the opinion that the submission was the result of a packaging problem for the company rather than a safety issue. They noted that there were a number of combination antitussive products which would be affected if a classification change were to occur. They felt that these products, which contained greater concentrations of theophylline than Nuelin Syrup, were appropriately classified as pharmacy-only medicines. In order to recommend a more restrictive classification, the Committee would require substantial supportive safety data. Neither the company submission nor the Ministry report had been able to supply such data and the Committee could see no reason for the reclassification of this product.

Recommendation

That there be no change to the current pharmacy-only classification of liquid theophylline.

(ix) Sennosides

The submission had been received from Reckitt & Colman and was for reclassification of sennosides from pharmacy-only to general sale medicines. These had been general sale medicines prior to 1991 but were classified as pharmacy-only medicines at that time in order to encourage the use of bulk laxatives by making the latter more readily available as general sale medicines while classifying stimulant laxatives as pharmacy-only medicines.

The Committee supported retaining the pharmacy-only classification of sennosides. All had seen instances of laxative abuse and inappropriate use. Members also agreed that early detection of bowel problems was desirable. For both cases they felt a derestriction in classification would make medical intervention one step more distant.

Recommendation

That there be no change to the current pharmacy-only classification of sennosides.

8 NEW MEDICINE FOR CLASSIFICATION

Amethocaine 4% for topical use (Ametop Gel, Smith & Nephew)

This was a new medicine application for a topical use for amethocaine. To date amethocaine had consent in preparations for internal and ophthalmological use only. Local anaesthetics had been reviewed in 1994. All topical applications were currently general sale medicines at 2% or less and pharmacy-only medicines above this strength.

There was no data to show that amethocaine was more toxic than any other local anaesthetic and members saw no reason not to classify this product in the framework already established for local anaesthetics.

Recommendation

That amethocaine for external use but not ophthalmological use be classified as a pharmacy-only medicine at strengths of more than 2%

9 MEDICINES CLASSIFIED BY THE MAAC

The Committee noted that the following new chemical entities had had classifications recommended by the Medicines Assessment Advisory Committee:

prescription medicines

atorvastatin
Adjunct to diet to reduce elevated total-cholesterol, LDL-cholesterol, and triglyceride levels in patients with primary hypercholesterolaemia, or mixed dyslipidaemia where the primary

abnormality is either elevated cholesterol or triglycerides. It is also indicated to reduce total-cholesterol and LDL-cholesterol in patients with homozygous familial hypercholesterolaemia.

irinotecan hydrochloride
For the treatment of patients with metastatic carcinoma of the colon or rectum whose disease is refractory to 5FU based therapy.

letrozole
For the treatment of advanced breast cancer in women with natural or artificially induced postmenopausal status, who have previously been treated with antioestrogens.

olanzapine
For acute and maintenance treatment of schizophrenia and other psychoses where positive symptoms and/or negative symptoms are prominent.

ropinirole hydrochloride
For the treatment of Parkinson's disease

stavudine
For the treatment of HIV infected patients (>5 months of age) for whom zidovudine treatment is not, or is no longer, appropriate.

Pharmacy-only medicine

etofenamate
For the treatment of rheumatic diseases of the soft tissue of the musculoskeletal system, eg muscular rheumatism, muscle spasms and painful stiffness of the shoulder (periarthropathia humeroscapularis), lumbago, sciatica, tenosynovitis, bursitis, diseases of the spinal column and joints caused by over-exertion or degeneration (spondyloses, arthroses) and blunt traumas (eg. Sports injuries, such as contusions, sprains and strains).

10 FOR THE NEXT MEETING

Members did not have any suggestions at that point for medicines which they considered suitable candidates for reclassification. It was agreed that any suggestions should be forwarded to the secretary by the end of June.

11 GENERAL BUSINESS

(i) The committee's expectations of the role of the pharmacist in the sale of restricted medicines and pharmacy-only medicines.

This document had been adapted from a report by the Canadian Drug Advisory Committee. It had been discussed at the previous meeting and sent out for consultation with interested bodies in August 1996.

General discussion followed of both the draft document and the feedback from interested bodies which had resulted from the consultation process. Members identified a number of problems and issues to be resolved and decided not to adopt the draft document dated June 1996 at that stage. There was general consensus that it was the role of the professional body to determine the way pharmacists operate and that the Ministry should liaise with the Pharmaceutical Society in the hope that the latter could produce a code of practice for the handling of restricted medicines and pharmacy-only medicines. The issue would be returned to the agenda of the next meeting.

Recommendation

That the Ministry work with the Pharmaceutical Society to produce a code of practice for the sale of restricted medicines and pharmacy-only medicines.

(ii) Date for October meeting

The Committee agreed to meet on Wednesday 15 October 1997 at 9:30am at the same venue.

The meeting closed at 2:50pm.