MINUTES OF THE ELEVENTH MEETING OF THE MEDICINES CLASSIFICATION COMMITTEE HELD IN THE FIRST FLOOR CONFERENCE ROOM OF THE DEPARTMENT OF HEALTH BUILDING 133 MOLESWORTH STREET WELLINGTON ON TUESDAY 29 JUNE 1993 COMMENCING AT 10:30AM

PRESENT

Dr S Martindale (Chair)
Ms L McLauchlan
Mr G Caves
Dr J Wilcox
Dr M Herbert
Mr R Griffith
Mrs C Smith (Secretary)

IN ATTENDANCE

Ms M Ewen
Dr S Jessamine (until 3pm)
Dr R Boyd (briefly after lunch)

1 WELCOME

Dr Martindale opened the meeting at 10:35am and welcomed members. She explained that this was to be the last meeting for Ms McLauchlan who had resigned from her employment with the Pharmaceutical Society. She announced that Ms McLauchlan was to be succeeded by Ms Ursula Egan who had been nominated by the Pharmaceutical Society and that all other committee members had been nominated to serve for a further three years of office. Dr Martindale thanked Ms McLauchlan for her services to the committee and wished her well in the future.

Dr Martindale then introduced to the committee Ms Margaret Ewen, Team Leader of the Utilisation Team and Dr Stewart Jessamine, new medical advisor to the Department and a member of both the Utilisation and Evaluation Teams. She explained that both had put considerable effort into preparing material for the meeting and would be invited to contribute to the areas in which they had been involved.

Thanks were expressed to the secretary and Utilisation Team for the work put into preparation of material for the meeting.

2 APOLOGIES

There were no apologies.

3 CONFIRMATION OF THE MINUTES OF THE TENTH MEETING

The minutes were confirmed and signed subject to the following amendments:

p1 the addition of the year, 1992, to the heading
p4 part B number vii should include the word "anti microbial" so that the entry reads "possible anti microbial resistance"

Dr Martindale suggested a change in procedure relating to the confirmation of the minutes. She pointed out that there was a very long time lapse between the meeting and the confirmation of the minutes and she was keen to receive members' comments within a much shorter time-frame. As it was necessary with the existing system to act upon the recommendations made in the minutes before they had been confirmed at the following meeting it was possible that the Department could act upon a recommendation which did not reflect the intention of the committee. It was agreed that minutes be sent to members for comment before being sent to the minister and that a date be set for the return of written comments. This way the minutes could be agreed upon much closer to the time of the recommendations and the Department could be sure that it was acting on the intention of the committee.

4 CORRESPONDENCE

There was one piece of correspondence. This was from the Family Planning Association asking what would be required in a submission to enable family planning nurses to prescribe contraceptives. The secretary explained she had referred the letter to those areas in the Department which were concerned with the issues of prescribing rights and contraception. Dr Martindale outlined the scope of the Prescribing Rights background paper being prepared by John Shaw and explained how it fitted in with the overall review of the legislation and the proposed role of MCC. She assured members that it was broad policy which was under consideration at this stage rather than the actual methods of implementation. She promised to keep the committee informed and perhaps to call in a speaker from the policy area at a later meeting.

5 OVERSEAS ISSUES

i Harmonisation with Australia

Dr Martindale brought the committee up to date on progress in this area. She explained that New Zealand now had two members on the Australian Drugs and Poisons Schedule Standing Committee(DPSSC) which looked at the scheduling of all poisons and also made recommendations on warnings. John Reeve, a toxicologist with the Ministry of Agriculture and Fisheries was one of the New Zealand members and she was the Department of Health member. So far she reported having been present at two meetings which each covered three days and dealt with a large agenda.

She said that the scheduling system for drugs and poisons was under review in Australia but that NZ hoped to have continued representation. There would therefore continue to be an opportunity for NZ to bring items to the agenda of the scheduling committee. With this in mind she thought it would be a useful exercise for a list to be compiled of the differences between the NZ and Australian schedules. In the interests of harmonisation moves could then be made either to reconsider our own classification of a medicine or to present it as an agenda item at a DPSSC meeting. She pointed out that the list of differences could be quite long and there would be a need to exercise a certain amount of caution as NZ tended to be ahead of Australia in considering products for rescheduling.

Members agreed that such a list should be compiled. They agreed that it was not necessary to have absolute alignment but that where there were differences the committee should be happy with the reasons for those differences.

ii Confidentiality of Reports

Dr Martindale explained that the DPSSC obtains much of its material from commonwealth advisory committees (ADRAC and ADEC). There is concern about the confidentiality of this material and members are required to surrender papers after their meetings. The DPSSC has discussed the problem of using the material but has not yet resolved the issue of needing to use agenda papers at state level to support committee recommendations. Dr Martindale said that NZ is seeking legal advice on its use of the material and that meanwhile the papers should be treated in confidence and returned at the end of the meeting. She hoped to be able to provide a firm policy on this by the next meeting and concluded that the problem might be solved by simply marking the papers "confidential" and treating them accordingly.

iii NZ and the World Scene

The secretary outlined a paper she had prepared at the request of the Associate Minister of Health, Maurice Williamson, asking why NZ medicines were not as readily available over the counter as in other countries, particularly Italy. She pointed out that a brief study revealed that NZ was in fact ahead in this area at the time the study was undertaken in October 1992 though there had been a few changes since that time. Members were updated on those changes known to have occurred.

The committee said they had found this information interesting as they too had thought that NZ was fairly restrictive.

Dr Martindale suggested that the Department should open up lines of communication with a selection of other regulatory bodies so that NZ could be kept up to date with classifications and classification changes in other countries.

Ms Ewen said that she felt the committee should also be looking at those medicines which are available OTC in other countries but which have not yet been made available in NZ. She went on to explain that NZ had become a world leader in OTC availability in recent years and that it was important that NZ look at the impact of these changes. She said that during the next financial year a project would be undertaken in the Department to look at the impacts of the recent changes in NZ. Ms Ewen told the committee that the end product would be a document suitable for international publication. She welcomed any future suggestions from the committee on suitable groups of medicines for consideration.

6 MATTERS ARISING

i H_2 Receptor Antagonists (cimetidine famotidine nizatidine ranitidine)

Dr Martindale reminded the committee that at the last meeting members had been in favour of making one or more of these medicines available other than on prescription. She asked the secretary to report on the situation in UK and USA. Neither country was reported as willing to reveal whether or not any of these medicines was under review. However, one company anticipated marketing its products OTC in these countries in the near future. Cimetidine and ranitidine were currently available OTC in Denmark.

Dr Martindale summarised the results of the investigation undertaken by Mr Griffith to determine outside response to a proposed reclassification. It was noted that the Society of Gastroenterology, the NZ Medical Association, Dr R S Stubbs of the Wakefield Surgical Clinic for Gastrointestinal Disease and Glaxo were against any relaxation of the prescription classification. The Ministry of Transport professed insufficient expertise in the area of the interaction of alcohol and cimetidine to offer an opinion. Lilly, Douglas and Pacific did not respond. Merck Sharp and Dohme was prepared to promote an OTC pack of famotidine and SmithKline Beecham would promote Contracid (200mg cimetidine)

Members found that this group of medicines scored well when considered in relation to the established criteria for OTC classification. Consumer convenience was rated as high and members saw no problems relating to potency, therapeutic index, toxicity or communal harm.

There was some discussion in the area of abuse potential. Members considered the possibility of medico-legal complications arising from drinkers using cimetidine as an excuse for high blood alcohol. The committee did not know of any documented evidence to support this being a problem. While they recognised that there could be a possible problem, members did not feel the issue was relevant to whether or not cimetidine should be sold OTC.

There was general agreement that the main area of concern was that of inappropriate use. This included use with NSAIDs and the masking of serious gastric conditions. Members felt that these could be dealt with as long as stringent requirements were imposed on the product information before a product was permitted to be sold OTC. They also felt the high cost of these medicines would limit their use to a considerable extent.

The committee felt that there should be warnings about the interaction of cimetidine with other medicines but, that the interaction of cimetidine with alcohol was unlikely to present a significant problem. This was because literature reports showed that cimetidine only appeared to affect blood alcohol when the dose of alcohol was low and was taken in the morning. The effect was shown to occur only in males and was small compared with the effect of fasting. There did not appear to be any enhanced effects on blood alcohol levels with higher intakes of alcohol. Members concluded that there would not be significant problems caused by the interaction of cimetidine and alcohol.

The committee agreed that the strength and pack size should be limited and that OTC indications should be clearly defined. A set of warnings for patients should be included with the package information. These warnings should be written up as guidelines for use by the evaluation team whenever an OTC presentation of an H_2 receptor antagonist is to be evaluated. The following recommendation was drafted and agreed upon subject to the Department finalising details. The companies are to draft patient information which is to be evaluated by the Department before an OTC presentation will be given consent to market. The patient information will also be made available for committee members. It was also considered desirable that pharmacists be provided with training material to reinforce the patient warnings and precautions.

Recommendation

That cimetidine, famotidine, nizatidine and ranitidine should become restricted medicines under the following conditions:

i sold in packs containing not more than 10 days' supply

ii contain not more than the approved recommended maintenance dose
This will probably be as follows but will be checked by the Department against material on file.

cimetidine	200mg twice a day
famotidine	10 mg twice a day
nizatidine	150mg twice a day
ranitidine	150mg twice a day

iii indications: the short-term treatment of dyspepsia or pain associated with hyperacidity not responding to antacids or as directed by a medical practitioner.

iv the following warnings are incorporated in package information:
- recommended only under medical supervision in patients over 40 years of age
- if symptoms persist beyond 5 days consult a doctor
- if there is a recurrence of symptoms with 2 weeks of completing the course consult a doctor
- concurrent use with NSAIDs should be undertaken only under medical supervision

ii Non-sedating antihistamines (astemizole loratadine terfenadine)

Loratadine had been placed on the agenda at the previous meeting as the committee had seen a place for one of the non-sedating antihistamines as a general sale medicine and considered loratadine the most suitable candidate for derestriction. Since that time the secretary had received a letter from the secretary of the Medicines Adverse Reaction Committee (MARC) recommending that the MCC consider reclassifying terfenadine, astemizole and loratadine as restricted medicines.

Members considered that there was no evidence at this stage to link loratadine with the other two antihistamines as there had been no reports of cardiac arrhythmias associated with loratadine in spite of very wide use. They could see no justification for recommending a change to the pharmacy-only classification currently held but would not recommend that it become a general sale medicine.

Concern was expressed about the use of Claratyne Syrup (loratadine) in infants under 2 years. It was decided that as this was a different issue it would be brought to the agenda of the next meeting.

The committee decided that although the possible cardiac side effects of astemizole and terfenadine were serious they were extremely rare. It was noted that no cardiac effects from either medicine had been reported in New Zealand. Members agreed that reducing the pack size would not reduce the risk. It was noted that New Zealand pack sizes are relatively small and that cost would be a limiting factor. Restricting the use to prescription medicine would also have little effect in reducing any cardiac side-effects as a doctor would be unable to tell if a patient would be likely to develop these side-effects.

Mr Griffith summarised material received from the Medicines Control Agency of Great Britain (MCA) supporting the changes they are about to make to the legal status of some of their non-sedating antihistamines. MCA are about to restrict the classification of loratadine and terfenadine which are currently OTC but which are about to become prescription medicines except in pack sizes containing 10 days' supply of 10mg dose for loratadine and 120mg dose of terfenadine. OTC sale of astemizole is already limited to 10 days' supply of 10mg dose and cetirizine is about to be released for OTC sale in packs of 10 days' supply of 10mg doses.

Members said they would like to know the reasons for the DPSSC decision at their last meeting to make no changes to the current scheduling of the non-sedating antihistamines. It was agreed that this information would be made available at the next meeting.

The non-sedating antihistamines cetirizine and mequitazine were not discussed.

Recommendation

That there be no change to the present pharmacy-only classification of terfenadine, loratadine or astemizole.

That loratadine syrup be considered at the next meeting.

That terfenadine and astemizole be kept under review for possible further restriction. The secretary is to write to the companies informing them of this and giving them time to comment in the light of the UK rescheduling and the MARC recommendation.

That MARC be asked to keep the committee updated on any further information on non-sedating antihistamines.

iii Nicotine in gum and patches

As decided at the previous meeting, the secretary had written to the New Zealand Psychological Society to see whether or not making nicotine in gum and patches available to registered psychologists through antismoking clinics would be helpful in making these products more readily available to those who required them. Their reply indicated that psychologists were more interested in using psychological than medicinal methods and that such a move would be of little benefit.

iv Codeine update

Dr Martindale told members that the views of both MCC and the Drugs Advisory Committee(DAC) had been sent to the Associate Minister. She said that he was in agreement with the MCC's concept of not wishing to prevent access for the majority but also wanted to alleviate the homebake problem. The Department had written to interested companies expressing the concerns of the DAC and asking for their comments on several issues. The replies were to be sent directly to the Minister's office by July 10. No feedback had been received by the Department at the time of the meeting but Dr Martindale promised to keep the committee updated on further developments. She added that the Australians did not appear to have a homebake problem and were looking at making codeine products more readily available.

v Reference list of specialist consultants

Committee members acknowledged that the Department of Health list was very outdated and it was decided that members would return to this matter at the next meeting when they had had more time to think about suitable candidates.

7 MEDICINES FOR CLASSIFICATION CONSIDERATION

i Topical tretinoin

Dr Martindale explained that this topic had come on to the agenda as a result of recent events in Australia. The Australian Adverse Drugs Reaction Advisory Committee had sent a report to the DPSSC who had in turn recommended urgent rescheduling of topical tretinoin for reasons shown in the summary document provided to MCC. NZ had also issued a media release warning women of child-bearing age that there is evidence to suggest a possible link between birth defects and use in early pregnancy of skin preparations containing tretinoin. The press release announced that the Department was to ask MCC to consider restricting topical tretinoin to prescription medicine.

Dr Martindale said the two companies marketing Airol and Retin-A had been contacted. She said that both companies would wish MCC to make a decision based on data and that both were surprised that there was not already a pregnancy warning on their product information. Both were asked to submit material for the meeting. Roche had nothing to offer and Janssen-Cilag had sent information the day preceding the meeting. Dr Jessamine had agreed to summarise the company data for members at the meeting.

Dr Martindale pointed out that at the time MCC rescheduled topical tretinoin from prescription to restricted medicine the pattern of changing use for photo damaged skin and for cosmetic reasons had not emerged.

The chairman pointed out the high level of concern in Australia regarding possible teratogenic effects as indicated by the unusual speed in which Australia had rescheduled topical tretinoin as a prescription medicine.

Dr Jessamine reported that the evidence supplied by Janssen-Cilag reviewed the evidence for teratogenicity of tretinoin and felt it was wanting. He said that several trials had been included showing no evidence of either accumulation of this medicine or of its metabolites, or of increased systemic absorption after prolonged use lasting up to one year. Systemic absorption of radio-labelled tretinoin produced circulating plasma levels approximately 100 times less than the level of the endogenous vitamin A analogue. The total circulating levels of both absorbed and endogenous analogue had been reported by the FDA as being in the order of 200 - 4000 times less than that for rats. Several population based studies in the USA have shown that there was no significant difference in the incidence of foetal abnormalities between women using tretinoin in pregnancy and the background incidence.

The Australians had suggested that absorption increased with use and that they had received reports of teratogenic effects which resembled those associated with oral retinoids

Dr Jessamine referred to human tests which showed no significant or foetal abnormalities but which were questioned by the Australians in that they were retrospective.

Members discussed at length the differences in the two sets of information but were not able to draw satisfactory conclusions as they felt the information was confusing. It was felt that the Australians regarded the four reported cases as being important enough to outweigh the company data supplied from the various trials. The committee noted that only one of the two reported Australian cases had the kind of birth defects associated with the oral dose of this medicine.

The committee debated the issue of patient information and agreed that some form of intervention other than labelling and package insert warnings was desirable but some members felt that pharmacists could perform this function equally as well as medical practitioners. Dr Martindale said that although the companies would probably agree to package warnings this could not be expected short-term as international packages were used. It was thought that the warning statement was a more important issue than that of classification.

Members did not wish to feel pressured by the press release to change the classification of topical tretinoin. However, it was acknowledged that according to public perception, a prescription medicine was to be treated more seriously than one which could be purchased OTC. They therefore decided to opt for caution and to recommend that topical tretinoin be reclassified as a prescription medicine.

Recommendation

That topical tretinoin be reclassified as a prescription medicine and that the companies be asked to include a suitable warning about use during pregnancy.

ii Aspirin for platelet aggregation

The committee did not see any reason why the indication for platelet aggregation should restrict the sale of 100mg aspirin. They felt that if the 100mg tablet were not readily available people wanting to use the product would be more likely to take a half or even a whole 300mg tablet daily than to buy a more expensive restricted medicine. Members felt that the 100mg enteric coated product already classified as restricted medicine should also be available as a general sale medicine. They did not specifically discuss the 300mg enteric coated product already on the market. Members were asked out of session to look at the classification of this 300mg enteric coated product and they agreed to recommend that this also be classified as a general sale medicine.

There was concern that a low-dose product could be considered as suitable for use for children and members wished to see a warning against use for children on the pack. This warning is already a legislative labelling requirement for aspirin.

Recommendation

That aspirin when indicated for platelet aggregation be classified in the same way as other aspirin.

That enteric coated aspirin in strengths of 300mg and less become general sale

That aspirin in enteric coated forms over 300mg and in slow release forms remain restricted medicine

iii Topical Minoxidil 5%

The preparation currently on the market was of 2% strength and classified as restricted medicine. Upjohn wished to promote a 5% strength of the same product.

One of the potential concerns with a higher strength was that of systemic absorption. However, members agreed that there was a reasonably measured dose administered by the devices supplied with the product and that there should not be a problem with accidental over-application. They saw the higher strength of topical minoxidil as still being a suitable medicine for the intervention of a pharmacist rather than a doctor in the sale. The committee wished to see the warnings against use with heart disease currently used in the 2% version continued in the 5% strength. They did not wish to see the stronger version of the product promoted as a first line of treatment.

Members decided that as there seemed no reason to make any change to the classification of topical minoxidil at this time, there was no need to make a recommendation on this agenda item.

iv Caffeine

Mr Griffith reported that he had investigated the effects of caffeine. If the daily doses were limited there appeared to be no problems although withdrawal headaches were possible. He was unaware of any restrictions on its sale in the USA although it was a prescription medicine in Australia when in combination with aspirin or paracetamol. There were some reservations about the fact that the product seeking consent to market would be sold door to door though it was noted that caffeine in combination with an analgesic had been available as a general sales medicine for many years. Members agreed that caffeine should remain available as a general sale medicine.

Recommendation That there be no change to the present classification of caffeine as a general sale medicine.

v **Coal Tar**

Members considered the research into tars done by Mr Griffith. They concluded that there was no reason to differentiate between coal and wood tars for therapeutic purposes and that they did not need to be looked at separately for classification purposes.

Members then considered the carcinogenic properties of tar. They agreed that there could be a distinction between medicines which were left on the skin and those which were removed but concluded that the risks were so slight that they saw no reason to restrict the sale of any tars at any strength.

Recommendation: That all tars are classified as general sale medicines and all reference to tars be removed from the First Schedule to the Medicines Regulations 1984

8 NEW MEDICINES FOR CLASSIFICATION

The following medicines have been recommended for classification as prescription medicines by the Medicines Assessment Advisory Committee:

cefpirome
paclitaxel
propafenone hydrochloride
sertraline hydrochloride

For classification by MCC

i **adapalene (Differin Pacific)**

This is a new active ingredient for the topical treatment of acne. New Zealand is the first country for which marketing application had been made. For these two reasons adapalene was seen to be suitable for classification as a prescription medicine.

Recommendation: prescription medicine

ii amorolfine hydrochloride (Loceryl, Roche)

Amorolfine is a topical antimycotic which belongs to a new chemical class. It was recommended for classification as a prescription medicine.

Recommendation: prescription medicine

iii azelaic acid (Skinoren, Schering)

This topical acne preparation has already been recommended as a prescription medicine as a result of postal consultation with members in April.

Recommendation: prescription medicine

iv gadodiamide (Omniscan)

The recommendation was for gadodiamide to be classified as a prescription medicine along with all other radiographic contrast media.

Recommendation: prescription medicine

v gentian compound concentrated infusion

Members could see no reason to restrict the sale of this product and recommended that it be classified as a general sale medicine.

Recommendation:general sale medicine

vi nicotine for nasal administration (Nicorette Nasal Spray, Kabi)

The committee agreed that there was a greater chance of overuse with the nasal route of administration than there was from patches or gum. For this reason they felt a restricted medicine classification would be appropriate.

Recommendation: restricted medicine

vii ciclopirox as a nail lacquer (Batrafen Nail Lacquer, Hoechst)

Ciclopirox is already classified as a pharmacy-only medicine for dermatological use. However it was felt that this product should be looked at as it was a new presentation of the medicine at a higher strength (8%) than any other on the market. Members noted that systemic absorption occurs and that serum levels can be detected. For this reason they felt that this particular product would be more suitably classified as a restricted medicine. It was agree that the Department would resolve the matter of how to amend the wording of the schedule to accommodate this recommendation.

Recommendation: restricted medicine

9 SUGGESTED ITEMS FOR CONSIDERATION FOR RECLASSIFICATION

Members had no suggestions for items for consideration for reclassification at the next meeting.

10 GENERAL BUSINESS

Dr Wilcox asked what had happened about the submission from the Podiatrists' Society requesting rights to prescribe certain medicines. Dr Martindale replied that this would be covered under the Prescribing Rights Project.

Ms McLauchlan asked whether a 2.5% lignocaine oral preparation would qualify as an external preparation. The secretary replied that this was so and explained the definition of "external use" in the Medicines Regulations.

The secretary asked that all claims be submitted by fax the following day so that costs of the meeting could be accrued to the current financial year. Actual claims forms and receipts could follow by normal post.

The meeting closed at 4:45pm