MINUTES OF THE SIXTEENTH MEETING OF THE MEDICINES CLASSIFICATION COMMITTEE HELD IN CONFERENCE ROOM SOUTH IN THE MINISTRY OF HEALTH BUILDING 133 MOLESWORTH STREET WELLINGTON ON 24 APRIL 1996 COMMENCING AT 9:30am

PRESENT

Dr S Martindale (Chairperson)
Mr R Griffith
Dr M Herbert
Dr J Wilcox
Mr G Caves (from 10:05am)
Mrs C Smith (Secretary)

IN ATTENDANCE

Dr G Boyd (1:00 - 1:45pm)
Dr S Jessamine (9:30am - 12:30pm)
Mr P Pratt (for Melatonin)

1 WELCOME

Dr Martindale welcomed members to the sixteenth meeting. She noted that three of the four non-Ministry of Health members had now completed their maximum service of six years on the committee and that this would be their last meeting. It was noted that Ms Egan had not been nominated for a further three-year term. Appointment of new committee members was yet to be finalised.

2 APOLOGIES

Ms Egan's apology for her absence due to overseas travel was noted. Her written comments on the agenda items were distributed to the rest of the committee.

Mr Caves sent an apology for a last-minute change of plan which necessitated his later arrival.

3 CONFIRMATION OF THE MINUTES OF THE FIFTEENTH MEETING

The minutes of the fifteenth meeting were confirmed as an accurate record of the meeting and were signed by the chairperson.

4 MATTERS ARISING

i Emergency Contraceptive Pill

Dr Jessamine reported the progress to date with the working party set up to implement the classification change recommended at the last meeting. It was noted that the Ministry had almost completed the plan for the project to develop package and consumer information requirements and educational material for pharmacists and consumers. A contractor had been engaged to manage the project and progress this work. The project was planned for completion by the end of August but it was hoped that the required amendment to the First Schedule of the Medicines Regulations 1984 would occur before that date. The first step in the project would be the drafting of the packaging and consumer information requirements. Consultation would then take place with those bodies who had expressed an interest in being involved. Discussions would also take place with the Pharmaceutical Society and the Pharmacy Guild about the educational resources necessary for pharmacists.

Dr Martindale told the committee that since the information had been released, considerable effort had been put into dealing with the reaction. While there had been no reactions on safety grounds, there had been considerable response from pro-life organisations and individuals and from politicians.

Dr Herbert pointed out that the classification change would still not make the ECP more readily available through practice and family planning nurses. Dr Martindale pointed out that such access could not be effected in the short-term as it would require a legislation change. The increased availability through pharmacists was a first step towards wider access.

Dr Wilcox stressed that the publicity surrounding the increased availability of the ECP should emphasise that pharmacies were an additional source of supply rather than an alternative to current sources.

ii Beclomethasone 50mcg for nasal use

This item had been deferred from the fifteenth meeting pending further information on use with nasal or sinus infection.

A paper from *The Journal of Family Practice*, 1986 vol 22 entitled *Probable Adrenal Suppression from Intranasal Beclomethasone* was tabled by Dr Wilcox who considered that there could well be other undocumented cases. Members considered that such cases could result only from long-term use.

No further evidence had been produced by pharmaceutical companies or by the Ministry to suggest problems with nasal or sinus infection during short-term use.

Mr Griffith commented that this type of therapy was the most effective treatment for seasonal rhinitis and that there would be public benefit from reclassification.

The committee agreed that any warnings or consumer information could be specified in the package insert. It agreed to recommend a reclassification to restricted medicine of beclomethasone 50mcg strength aqueous nasal spray for use in persons over 12 years of age for the treatment of allergic rhinitis when in an OTC-specific pack approved by the Director-General for sale as a restricted medicine. The pack should contain no more than 200 doses and warnings should be included against long-term use, use with infection and concurrent use with other similar steroids. Information on when to seek medical advice should also be included. The package information details required for over-the-counter use would be finalised by the Ministry.

Recommendation

That beclomethasone 50mcg aqueous nasal spray be reclassified as a restricted medicine when:

- in a pack approved by the Director-General of Health for sale as a restricted medicine
- indicated for the short-term treatment or prophylaxis of allergic rhinitis
- for persons aged 12 years or more
- in a pack size of no more than 200 doses
- a maximum daily dose of 200mcg applies
- accompanied by warnings and consumer information as required by the Ministry including information on when medical advice should be sought and warnings against long-term use, concurrent use with other steroids and use with nasal or sinus infection

5 SUBMISSIONS FOR RECLASSIFICATION

i Nedocromil (Tilarin Nasal Spray Tilavist Eye Drop, Fisons)

The submission made by the Ministry was for reclassification from prescription medicine to pharmacy-only medicine of nasal and ophthalmological forms in order to bring the classification into line with that of sodium cromoglycate. The submission had been deferred from the fifteenth meeting at the request of the company. Fisons had subsequently expressed opposition to a reclassification for over-the-counter sale. While the committee saw no safety issues to prevent the reclassification it acknowledged that, in view of the company's wishes and the current OTC availability of sodium cromoglycate, an alternative product, there was no compelling reason to reclassify this medicine in the absence of company support.

Recommendation

That there be no change to the current prescription medicine classification of nedocromil sodium.

ii Corticosteroids for the treatment of allergic rhinitis

A paper had been prepared by the Ministry reporting on budesonide, flunisolide, betamethasone and fluticasone as possible candidates for over-the-counter sale. This would complete the investigation of this group of medicines for reclassification.

The committee accepted the Ministry view that although betamethasone was the oldest of this group of medicines, there had been reports of iatrogenic HPA suppression in adults and one case of Cushings syndrome. Due to these reports and the fact that the only available betamethasone aqueous nasal spray was combined with a vasoconstrictor, the committee did not feel that betamethasone should be reclassified unless the NZ agent were to make a formal submission containing detailed and acceptable safety data.

Members felt that fluticasone was still too new to be made available over the counter and that they would prefer to review safety data submitted by the company before considering it further for reclassification.

The committee agreed with the Ministry report that there was sufficient evidence to support the reclassification of budesonide and flunisolide as restricted medicines. These should be treated in the same way as beclomethasone and be sold in OTC-specific packs for short-term use with warnings and other package information to be finalised by the Ministry.

Recommendations

That betamethasone and fluticasone remain prescription medicines.

That flunisolide and budesonide aqueous nasal sprays be reclassified as restricted medicines when:

- in packs approved by the Director-General of Health for sale as restricted medicine
- indicated for the short-term treatment or prophylaxis of allergic rhinitis
- for persons aged 12 years or more
- in a pack size of no more than 200 doses
- accompanied by warnings and consumer information as required by the Ministry including information on when to seek medical advice and warnings against long-term use, concurrent use with other steroids and use with nasal or sinus infection
- the following maximum daily doses were applied:
  flunisolide: 200mcg for adults and 150mcg for ages 12-16 yrs
  budesonide: 400mcg

iii Aciclovir (Zovirax Cold Sore Cream, Parke Davis-Wellcome)

This was a company submission for reclassification from restricted to pharmacy-only medicine. Aciclovir for external use but not for ophthalmological use had been reclassified from prescription to restricted medicine in 1991

The committee agreed unanimously that this was a suitable candidate for reclassification as a pharmacy-only medicine. Members thought that any necessary instruction could be dealt with in the package information. They agreed that the Ministry should be left to word the scheduling of topical aciclovir to preclude its OTC use for genital herpes.

Recommendation

That topical aciclovir for the treatment of cold sores be reclassified as a pharmacy-only medicine.

iv Amyl nitrite

The Ministry had requested exemption from pharmacy-only classification for this medicine when sold from outlets licensed under the Toxic Substances Regulations 1983 to sell sodium cyanide paste for the purposes of vertebrate pest control. This would legitimise the current practice of selling amyl nitrite as an antidote to cyanide poisoning from the same outlets as sodium cyanide for pest control.

The committee agreed to recommend the exemption.

Recommendation

That amyl nitrite be exempt from pharmacy-only classification when sold from outlets licensed under the Toxic Substances Regulations 1983 to sell sodium cyanide paste for the purposes of vertebrate pest control.

v Azelaic acid (Skinoren, Schering)

On the basis of the company safety data and the Ministry report, the committee agreed to recommend the reclassification of azelaic acid from prescription to pharmacy-only medicine. It was noted that although this was an older product, its use was relatively new in New Zealand. The comment was made that users needed to be persistent with their use of the product to achieve acceptable results but no need was seen for pharmacist intervention in the sale.

Recommendation

That azelaic acid be reclassified from prescription to pharmacy-only medicine.

vi Diclofenac (Cataflam, Ciba)

This company submission was for the reclassification of 25mg tablets or capsules from restricted to pharmacy-only medicine when in pack sizes of not more than 30 tablets or capsules.

Mr Griffith pointed out that there were other medicines in this group with a better safety profile than diclofenac and that derestriction would lead to increased usage. The committee considered that New Zealand was already well-provided with OTC analgesics.

An article from *Time,* April 1996 entitled *Bitter Ad to Swallow* was distributed to the committee. Members were aware of this analgesic advertising battle taking place in the USA and did not wish to see New Zealand become involved in a similar situation.

There was no support for a change to the present classification.

Recommendation

That there be no change to the current classification of diclofenac.

vii Naproxen sodium (Aleve, Roche)

This was a company submission for the reclassification of a 220mg tablet as either a general sale or a pharmacy-only medicine with unrestricted indications.

As for diclofenac, there was no support for a reclassification of naproxen sodium.

Recommendation

That there be no change to the current classification of naproxen sodium.

viii Fluconazole 150mg capsule (Diflucan, Douglas)

This company submission was for the reclassification from prescription to restricted medicine for a single-dose oral capsule for the treatment of vaginal candidiasis.

Dr Wilcox distributed a paper summarising his views on the unsuitability of this medicine for self-medication.

The committee agreed that it would not support reclassification. Topical rather than oral treatment was seen as first-line and members agreed that New Zealand was well supplied with OTC topical preparations. Experience with single-dose use of fluconazole was quite limited in New Zealand amongst general practitioners. While

this product might have some consumer appeal over a topical application, the view of the committee was that safety of the high dose used in single administration had not been adequately shown for self-treatment of a common and recurrent condition. It was considered that the possibility of hepatic toxicity was still too high for such wider use to be recommended. The committee agreed that it could possibly review the situation when more safety data and New Zealand experience was available.

Recommendation

That there be no change to the prescription medicine classification of fluconazole.

ix Propylene glycol

x Isopropyl myristate

The Ciba submission for the reclassification of these two substances was accepted unanimously by the committee on the basis of information contained in the Ministry report.

Recommendation

That propylene glycol and isopropyl myristate become general sale medicines.

xi Antimicrobial mercurials

The item was removed from the agenda on the grounds that it was not a classification issue.

xii Melatonin

Melatonin had recently been declared a medicine by the Ministry and an urgent consideration of its classification had been requested. Mr Pratt explained that the melatonin of concern was a synthetic preparation of a hormone produced naturally by the pineal gland. A number of products containing melatonin had appeared bearing therapeutic claims while others had relied on information in the public domain to inform people of therapeutic uses. Although melatonin was present in some foods at low levels it could not be regarded as a dietary supplement as it was taken only for therapeutic purposes. Mr Pratt added that very little was known about melatonin as it had not been subjected to close scientific scrutiny. As it had not been subjected to any pharmaceutical regulatory approval process there was no confidence in the safety and manufacturing quality of products. Nor was there any information to support the doses available. These appeared far in excess of the doses suggested as effective in

the position statement on melatonin from the New Zealand National Nutritional Food Association. Copies of this statement were distributed to members.

Dr Martindale pointed out that, as an unapproved medicine, melatonin could legally be available from natural health practitioners if it remained unscheduled. Any classification change would have the impact of making it unavailable for supply in this way.

The committee was provided with copies of a letter from Health Canada outlining action taken in Canada to classify melatonin as a prescription drug. No submission had been made in Canada to market a drug containing melatonin.

It was also noted that Italy, Denmark, France, the UK and Belgium had already taken some form of action to prevent the supply of melatonin as an unregistered medicine.

The committee decided that, as melatonin was a hormone and there was insufficient information available for a judgement to be made about its safety, it was appropriate that it should only be supplied on the prescription of a qualified medical practitioner.

Recommendation

That melatonin be classified as a prescription medicine.

xiii Ipecacuanha

The committee accepted the Ministry proposal to amend the schedule in order to correct an earlier error.

Recommendation

That ipecacuanha be classified as a pharmacy-only medicine in medicines containing 0.05% or more of emetine

That emetine be classified as a pharmacy-only medicine in medicines containing 0.05% or more

That ipecacuanha be a general sale medicine in medicines containing less than 0.05% of emetine.

That emetine be a general sale medicine in medicines containing less than 0.05%

xiv Terfenadine and astemizole

The Medicines Adverse Reactions Committee (MARC) had requested that these be reclassified as restricted medicines due to the risk of ventricular arrhythmias. The matter had been discussed in June 1993 after a request from the MARC for consideration for reclassification to restricted medicine of terfenadine, astemizole and also loratadine. At that time the committee did not consider reclassification was justified because of the rarity of the adverse effect.

On the basis of the evidence presented in the more recent MARC report, the committee acknowledged that there was now sufficient evidence available to indicate that terfenadine and astemizole were less safe than loratadine or cetirizine in that the former had been found to be associated with prolongation of the QT-interval and torsade de pointes.

In view of the high sales volumes the committee saw potential problems in recording sales if these medicines were to be reclassified as restricted medicines. Except in the case of adverse events triggered by drug interactions, the committee did not see the intervention of a pharmacist or a doctor in the supply of terfenadine or astemizole as able to improve the outcome for those few consumers who would suffer adverse reactions. However, it agreed that pharmacist intervention could emphasise the increased risk associated with these agents and could reduce the risk of consumers experiencing these life-threatening adverse events when triggered by interactions with other commonly used medicines or the use of excessive doses.

The committee therefore agreed to recommend that terfenadine and astemizole become restricted medicines.

There was some concern about the adverse cardiac reactions reported with loratadine and cetirizine and it was agreed that the MARC should be asked to actively seek further information on these other non-sedating antihistamines.

Recommendation

That terfenadine and astemizole be reclassified from pharmacy-only to restricted medicine.

xv Paracetamol

a A Pharmaceutical Society submission for the reclassification of single-ingredient solid-dose products from general sale to pharmacy-only medicine.

b A submission from SmithKline Beecham for an increase from 10 grams per pack to 12.5 grams or 25 units for general sale and for harmonisation with Australian scheduling.

c Dr Martindale told the committee that there was now a third consideration as there had been an application for the approval of a **junior soluble paracetamol tablet** which would also need to be considered for classification.

a Pharmaceutical Society submission

Mr Caves spoke to the Pharmaceutical Society submission and while he said that he would prefer to see paracetamol available only from pharmacies, he was not convinced of the need to reclassify.

Ms Egan's written report did not support reclassification.

Other committee members were also in favour of retaining the current classification on the grounds that the potential toxicity from improper use should not preclude people from being able to buy paracetamol. Members noted that much larger quantities could be bought from pharmacies without advice from a pharmacist and doubted that there would be a gain from a reclassification of the nature proposed by the Pharmaceutical Society.

Dr Martindale remarked that the submission was a potent argument for changing the warnings on the pack rather than for reclassifying the medicine. It was also noted that advertising guidelines would be a more effective way of dealing with multiple pack promotions.

b SmithKline Beecham submission for increased general sale pack size

Mr Griffith pointed out that the current 10 gram pack size set earlier as the limit for general sale had been chosen as it was safely below a total dose likely to cause hepatoxicity in healthy adults. It was noted that 15 grams is considered the approximate amount required for a potentially toxic dose.

In the light of this, members considered that the submission, being on economic rather than on safety grounds, was not compelling and agreed that the pack sizes should remain at 10 grams for general sale classification.

c Panadol Junior Soluble Paracetamol

Dr Martindale explained that there was a new medicine application for a 250mg soluble tablet with doses of 250mg to 500mg for children aged 6-12 years. She said that this was the first application for a paediatric solid-dose preparation and that under the current regulations this would be a general sale medicine.

The committee showed some concern about the palatability of the product but agreed that a tailor-made product was safer than dividing an adult preparation. It was noted that liquid paracetamol was available only from pharmacies but that the liquid

preparation was aimed at ages of less than 6 years as well. Members agreed that the soluble junior tablet should be available as a general sale medicine but were unhappy for it to be recommended for use in children under 6 years of age. However, they felt that this could be dealt with in guidelines rather than as a classification issue.

Paracetamol labelling issues

Dr Martindale informed the committee that the Therapeutics Section was currently preparing a guideline document on paracetamol for inclusion in the revised *New Zealand Regulatory Guidelines for Medicines*. It was intended that these guidelines be brought to the attention of all companies marketing paracetamol.

Clarity was being sought in the guidelines on paediatric doses. The committee agreed that it would be happy for paediatric doses to be restricted to 120mg tablets and for instructions not to divide tablets to be included. The Committed wished the warning against use in children under 2 years to be made consistent with the dose instructions on packs.

The committee also felt that the Ministry should look carefully at the warning statements and perhaps consider the required Australian warnings for paracetamol. It suggested that there should be a warning about the potential for liver damage with alcohol use or abuse.

Recommendation

That there be no change to the current classification of paracetamol.

6 NEW MEDICINES FOR CLASSIFICATION

Sodium picosulphate (Pico Salax Rhone Poulenc Rorer)

The committee concurred with the Ministry report recommending that this laxative would be appropriately classified as a pharmacy-only medicine along with bisacodyl.

Recommendation

That sodium picosulphate be classified as a pharmacy-only medicine.

Medicines classified by the MAAC

Prescription medicines
anastrazole
azelastine hydrochloride
cisatracurium besylate

docetaxel
lamivudine
saquinavir mesylate
sevoflurane
tamsulosin

Pharmacy-only medicine
Lodoxamide trometamol for ophthalmological use.

Members had no queries relating to the classifications recommended by the Medicines Assessment Advisory Committee.

Recommendation

That the above medicines be classified according to the recommendations of the MAAC.

7 FOR THE NEXT MEETING

Suggested items for consideration

i levocabastine as suggested by Janssen Cilag for reclassification from restricted to pharmacy-only medicine.

There were no further suggestions at this point for consideration at future meetings.

8 GENERAL BUSINESS

i Revised statement of factors for the classification of medicines

The committee had requested at the fifteenth meeting that the Ministry work on a revision of the current criteria for classification to bring the New Zealand criteria for classification and reclassification closer to factors outlined in the Canadian Drug Advisory Committee Report on harmonised schedules in Canada.

Members considered the draft paper prepared and tabled by Dr Martindale. This was based on the Canadian document and reference had also been made to Australian criteria for classification.

Dr Martindale said that she felt the Canadian document appeared to capture what New Zealand had been trying to achieve with its criteria for classification and she thought it would be useful if the committee could have a more systematic method of guiding itself through the scheduling of medicines. She suggested that the Ministry prepare a further draft, revised in the light of comment by current committee members, to

circulate for external consultation and that the results be brought to a later meeting of the committee.

A minor adjustment was made to the draft document in order better to reflect regional needs of the New Zealand population such as allergic rhinitis.

It was agreed that members should study the draft document and return any comments to the secretary by the end of the following week.

Dr Martindale said that she thought it would also be useful if the committee could issue a statement of its expectations of the role of pharmacists in the sale of restricted and pharmacy-only medicines. This could be used not only as a signal to pharmacists but also to advise consumers of the level of service and pharmacist intervention they should reasonably expect. A document of this type would also be of assistance to others making submissions to the committee.

The committee then reviewed and discussed the Canadian material and reached agreement on the changes to be incorporated into a draft to be circulated for external consultation with interested parties including the Consumers Institute. It was suggested that the UK protocols for pharmacists also be considered during the further development of the document.

Recommendations

That a revised statement of factors for classifying medicines be circulated by the Ministry as a draft document for consultation with those bodies normally consulted on medicines guidelines and, when finalised, the material should be incorporated into the *New Zealand Regulatory Guidelines for Medicines*.

That a document be drafted by the Ministry outlining the Medicines Classification Committee's expectations of pharmacists in the sale of pharmacy-only and restricted medicines and that a draft document should be sent out for consultation in the same way as the statement of factors for classifying medicines.

ii Evaluation of submissions to the committee

At the fifteenth meeting the committee requested that the Ministry investigate whether or not a workable proposition could be devised for committee members to conduct literature searches to evaluate submissions for classification or reclassification.

Dr Martindale reported that there was no practical way to do this as there was no money available to recompense members for time spent. She said that the most practical approach at this stage would be to try and improve the quality of material submitted by companies and to ensure that Ministry evaluators probed as deeply as possible into the topics in the course of preparing their reports.

iii Impact of the reclassification of prescription medicines to restricted medicines.

A report prepared by David Buckle on the results of the survey conducted by the Therapeutics section had been sent to the committee. Members commented that they had not received a copy of the survey itself and would be interested to do so. Dr Martindale replied that although the results of the survey had been intended for publication the study had turned out to be quite small, probably reflecting the low sales volumes of the medicines concerned. She said that there was also some concern that parts of the survey relied on the recall of patients and doctors and that it had been decided not to proceed with publication at that point. She reported that the overall patterns of the study showed that consumers were pleased about increased access to the medicines in the study, that there had been no evidence of harm to consumers from the increased availability and that consumers did not tend to recall being advised on the use of the medicine at the point of sale.

It was agreed that the secretary should forward copies of the survey to the committee and that the survey should be kept confidential as a decision had not yet been made on whether or not it would be published.

Closing remarks

Dr Martindale thanked members for their six years of service to the committee. She said that she had enjoyed the association and appreciated the support of members in the development of some landmark recommendations and in the development of a set of criteria for making classification recommendations.

Members expressed their thanks to the chair and made special reference to her skill in achieving recommendations on a consensus basis. Members also thanked the secretary for the quality of service provided to the committee.

The meeting closed at 3:15pm