

Minutes of the National Drug Scheduling Advisory Committee Meeting December 3-4, 2006

A meeting of the National Drug Scheduling Advisory Committee (NDSAC) was held on Sunday and Monday, December 3-4, 2006 at the Lord Elgin Hotel, 100 Elgin St., Ottawa.

Participants:

NDSAC Members: Margot Priddle (Chair), Dawn Frail (Vice-Chair), Dr. Anita Carrie, Phil Hudson, Dr. Sheldon Koven, Dr. Larry Lynd, Dr. Nancy MacDonald, Dr. Ruth Wilson

Observers: Micheline Ho, Joan Sayer, Karen Wolfe (Dir Phm Pract Supp, NAPRA)

Staff: Norma Lynn Pearson (Drug Information Specialist, Ottawa Valley Regional Drug Information Service), Ken Potvin (Exec. Dir., NAPRA)

Guests: **Pfizer Consumer Healthcare:** Praveen Chawla (Director, Regulatory Affairs), Philloza Suleman (Manager, Regulatory Affairs), Robert Milne (Manager, Medical Information & Safety), Robert Marsala (Manager, Regulatory Affairs)

J&J-Merck Consumer Pharmaceuticals: Brenda Wilson (Manager, Regulatory Services), Todd Breedon (Director, Regulatory & Scientific Affairs)

Sunday December 3, 2006

1.0 Call to Order, Opening Remarks and Welcome of New Members

Chair M. Priddle called the meeting to order at 9:05 am on Sunday December 3, 2006 and invited the new Committee members, Dr. Anita Carrie and Dr. Nancy MacDonald, to introduce themselves. A roundtable of introductions of other participants followed.

1.1 Conflict of Interest Declarations

The Chair called for Committee members to declare any real or perceived conflicts of interest. L. Lynd noted that he had a project ongoing with a grant in aid from Pfizer, as per prior disclosures. While he has complete autonomy for the research, Dr. Lynd indicated that he would excuse himself from deliberations on the Pfizer products. P. Hudson noted that he had an arms length relationship with Johnson & Johnson, and would therefore excuse himself from deliberations on famotidine. N. MacDonald reported that she had been employed by Johnson & Johnson in the past and is familiar with the presenters from this company. As she has been retired for three years from this employment, it was the consensus of the Committee that Dr. MacDonald would be able to participate in the deliberations.

2.0 Approval of the Agenda

On a motion by L. Lynd, the Agenda was approved as circulated.

3.0 Approval of the Minutes of the June 2006 NDSAC Meeting

It was noted that the Minutes from the June 2006 NDSAC meeting had been approved by electronic voting of the meeting attendees, and had been subsequently posted on the National Association of Pharmacy Regulatory Authorities (NAPRA) website.

4.0 Committee Membership

K. Potvin noted that Margot Priddle had been reappointed to a second three-year term, by NAPRA's Executive Committee, for the period October 2006 – October 2009.

5.0 Definition of "Marketed"

K. Potvin provided background information on this item, and reported the feedback received from external stakeholders through the public consultation process. It was noted in the discussion that Canadian Internet content falls within the jurisdiction of the Food and Drugs Act. For information only.

6.0 NAPRA Policy for NHPs

K. Potvin provided an update on the NAPRA policy with regard to natural health products (NHPs) and the National Drug Schedules (NDS). Health Canada has committed to looking at a regulatory amendment to ensure that products licensed as NHPs meet the criteria for safe self-care and self-selection. M. Ho noted the difficulties in defining "self-care". K. Potvin clarified that any product regulated as a homeopathic medicine (DIN-HM) would be encompassed by the NAPRA Policy for NHPs. D. Frail described the challenges in communicating the importance of this matter to decision makers within the governments. Variable reactions to the Policy from the provincial governments could ultimately result in a loss of harmonization of the conditions of sale of NHPs. It was suggested that NAPRA draft a letter for use by the PRAs in communicating with their governments. The message must be simple and consistent across the jurisdictions.

7.0 Format Options for Drug Scheduling Review Submissions

M. Priddle opened the discussion on the new process for receiving and distributing the drug scheduling review submissions. There was considerable feedback, most of it favourable, that will be considered by the NAPRA office for the next meeting. Specifically, the companies will be asked to provide an MS Word version of the submission, so that the Committee members are able to insert comments or highlight sections for their reference. The official requirements as posted on the NAPRA website will be amended once the optimal process has been identified.

8.0 Meeting Dates for 2007

After a survey of NDSAC, and brief discussion at this meeting, the following dates were confirmed as the NDSAC Meeting Dates for 2007:

March 4/5; June 10/11; Sept 16/17; Dec 2/3

These dates will be published on the NAPRA website, along with the submission deadlines.

9.0 Preparation for Drug Scheduling Review Discussions

The Committee discussed a number of general questions and considerations pertaining to the drug scheduling review submissions brought to this meeting, in preparation for the presentations.

10.0 Request for Unscheduled Status for Oral Famotidine and its Salts, 20 mg

Representatives from Johnson & Johnson-Merck Consumer Pharmaceuticals made a presentation to the Committee to support their request to have *oral 20 mg famotidine and its salts* assigned a status of Unscheduled, pending federal deregulation per Project No. 1496. P. Hudson and N. MacDonald excused themselves from this portion of the meeting. The presenters noted that Johnson & Johnson had purchased Pfizer Consumer Healthcare in June 2006, but that the acquisition had not been fully completed as yet. There were a number of aspects of the submission that appealed to the Committee Members, including the Pharmaceutical Safety and Efficacy Assessment Report from the Therapeutic Products Directorate (TPD). This document was considered by the Committee to be well written and very helpful.

There was considerable discussion about the potential for masking of more serious conditions (e.g. gastric carcinoma) and warnings in the Product Monograph that middle-aged patients with new or changed dyspeptic symptoms should consult their physician prior to commencing therapy. There was also some reluctance to accept that doses of 20 mg were more effective than 10 mg, and concern that patients would increase to 40 mg dosing to obtain relief with more severe symptoms. The company representatives affirmed that their intention was to continue to market both the 10 mg and 20 mg products. There was discussion with the representatives about the prospect of limiting package size to correspond to the maximum recommended duration of treatment prior to medical consultation.

In the NDSAC deliberations following the formal presentation and discussion, it was noted that package inserts and labeling may be sufficient for English speaking patients with good eyesight, but that the role of the pharmacist may be increasingly important for ethnic or elderly populations. A package size restriction, as had been suggested by the company representative, was discussed at length. The Committee asked NAPRA staff for additional information on famotidine 10 mg products that are already on the market, and deferred further discussion until this information could be provided on Monday December 4th.

The requested information was provided to NDSAC, and allowed the Members to determine an appropriate strategy for addressing concerns about long term use, particularly in populations at risk of inappropriate use. While a 14 day treatment course was the maximum that was recommended on the labeling, the current availability of some consumer products with 60 tablets of 10 mg was also considered.

The Committee agreed that the following scheduling factors were applicable to these products intended for self-selection: Schedule II – Factor #6, Schedule III – Factors #1, #2, and #4.

It was moved by D. Frail that “famotidine and its salts, when sold in preparations for oral use containing 20 mg or less of famotidine per dosage unit and indicated for the treatment of heartburn, in package sizes containing no more than 600 mg of famotidine” be Unscheduled (pending federal deregulation).

The motion was carried after debate.

The schedule status of package sizes containing more than the established limit of 600mg was then discussed. The primary concern was ongoing use of such products without a diagnosis, where the involvement of a pharmacist may be the primary access point for referral to a physician. In reviewing the scheduling factors, the following were felt to be applicable by the Committee: Schedule I – Factors #1 (qualified, for indications other than heartburn that patients may not be able to distinguish from heartburn) and #2; Schedule II – Factors #1, #5, #6 and #8; Schedule III – Factors #1, #2 and #4.

It was moved by R. Wilson that “famotidine and its salts, when sold in preparations for oral use containing 20 mg or less of famotidine per dosage unit and indicated for the treatment of heartburn, in package sizes containing more than 600 mg of famotidine” be moved to Schedule II (pending federal deregulation).

The motion was carried.

There was subsequent discussion on the schedule status of antacids, and the opportunity for long term use without health professional intervention (particularly when these are regulated as NHPs). While there were some considerations raised with the impracticality of consuming large doses of liquid antacids, in order to get the same symptomatic relief as with the H₂-antagonists, the matter was not resolved. The scheduling factors had been reviewed in the context of the drug review submission at hand.

11.0 Request for Change in Schedule Status from III to Unscheduled for Oral Diphenhydramine and its Salts, for Adults and Children 6 years of age and Older

Pfizer Consumer Healthcare representatives made a presentation to support their request for Unscheduled status for *oral diphenhydramine and its salts, for adults and children 6 years of age and older*.

After reviewing the documents submitted, hearing the company's presentation, and obtaining further information during the question period, NDSAC members deliberated on the submission. The Committee spent considerable time discussing the risks associated with the use of diphenhydramine (DPH), particularly in the elderly and in the context of its use as a sleep aid. It also noted the wide variety of products in the cough and cold category, and the confusion this creates for consumers when selecting an appropriate product. The pharmacological and side effect profile of DPH, and consequently its approved indications, were considered sufficiently distinct from those of chlorpheniramine as to question the validity of such a comparison.

N. L. Pearson provided some of the original references cited in the letter that had been received from the Ontario Pharmacists' Association's Drug Information and Resource Centre. The studies suggested that there was lower abuse potential for DPH than dimenhydrinate, and that gel caps were the most significant issue for high risk populations such as schizophrenics. This drug was not recommended for routine use in the elderly, according to some sources, due to side effects such as delirium, cognitive impairment, and urinary retention.

In reviewing the scheduling factors, the Committee identified the following as applicable: Schedule III, Factors #1, #2, #4, #5, #6 and #8.

It was moved by R. Wilson that "diphenhydramine and its salts and preparations (except for parenteral or topical use" remain in Schedule III.

The motion was carried after debate.

12.0 Request for Unscheduled Status for Oral Ranitidine and its Salts, 150 mg

Pfizer Consumer Healthcare representatives presented their case for Unscheduled status for *oral ranitidine and its salts, 150mg*, pending federal deregulation. In the discussion period that followed, the NDSAC members further inquired on the dosing issues, and the potential for masking more serious disease as had been discussed with famotidine. The members asked for additional information from NAPRA staff on the package sizes for ranitidine 75 mg products currently on the market, and deferred further discussion until Monday December 4th.

Upon reviewing the findings of the search of Health Canada's Drug Product Database, the Committee agreed that a package size restriction of 4500 mg would be reasonable. In considering the scheduling factors, the following were deemed to be applicable to these products intended for self-selection: Schedule II – Factor #6, Schedule III – Factors #1, #2, and #4.

It was moved by D. Frail that "ranitidine and its salts, when sold in concentrations of 150 mg or less per oral dosage unit and indicated for the treatment of heartburn, in package sizes containing no more than 4500 mg of ranitidine" be Unscheduled (pending federal deregulation).

The motion was carried.

The schedule status of package sizes containing more than the established limit of 4500 mg was discussed in concert with the deliberations on larger package sizes of famotidine. In reviewing the scheduling factors, the following were felt to be applicable by the Committee: Schedule I – Factors #1 (qualified, for indications other than heartburn that patients may not be able to distinguish from heartburn) and #2; Schedule II – Factors #1, #5, #6 and #8; Schedule III – Factors #1, #2 and #4.

It was moved by R. Wilson that “ranitidine and its salts, when sold in concentrations of 150 mg or less per oral dosage unit and indicated for the treatment of heartburn, in package sizes containing more than 4500 mg of ranitidine” be moved to Schedule II (pending federal deregulation).

The motion was carried.

13.0 Review/Pilot of Proposed Revised Scheduling Factors

The Committee utilized the most recent version of the revised scheduling factors, slightly modified after the experience at the June 2006 NDSAC meeting, as the second of three pilot tests. Each of the drug scheduling review requests was subjected to the new scheduling factors, and the Committee identified some further improvements to the draft document. The revised version will go through one more iteration of testing, and will then be submitted to NAPRA’s Executive Committee for consideration in advance of a public consultation process.

The meeting was adjourned at 4:30 pm.

Monday December 4, 2006

14.0 Call to Order

Chair M. Priddle called the meeting to order at 9:10 am on Monday December 4, 2006.

15.0 Content of Submissions – Consideration of CIOMS Criteria

L. Lynd reported that there had not been any progress on this item since the last meeting, and that comments on the previously circulated document were still welcome. K. Potvin will ensure the document from the June 2006 NDSAC meeting is provided to the Committee, and a reminder to provide comments to L. Lynd by January 15, 2007 will be issued early in the new year. Dr. Lynd will then prepare a document for discussion at the March 2007 NDSAC meeting.

M. Ho noted that if the sponsor requests the Pharmaceutical Safety and Efficacy Assessment Report, they would get it, but if a third party sought this they would have to submit an access to information request. The advice to NDSAC is therefore to ask the company to request the report and provide it to NDSAC, as part of the submission requirements.

16.0 NAPRA Website Redevelopment

K. Potvin provided a brief overview of NAPRA's initiative to review its website, and encouraged everyone to respond to the online survey.

17.0 TPD Schedule F Amendment Proposals: Proposed Additions to Part I of Schedule F

Several Schedule F regulatory amendment proposals were brought forward to NDSAC for information. These included:

Project #1491 – Deracoxib

Project #1478 – Resocortol and its derivatives

Project #1502 – Histrelin and its salts; Solifenacin and its salts; Trosipium chloride

Project #1511 – Pregabalin and its salts and derivatives

Project #1512 – Abatacept; Entecavir; Sunitinib and its salts

Project #1441 – Zaleplon

Project #1508 – Nicotinic Acid was discussed in detail as it has an impact on the NDS. At the September 2005 NDSAC meeting, the following Initial Recommendation was made, pending the finalization of the proposed regulatory amendment as per Project #1451 at that time:

Niacin (Nicotinic Acid) and its salts and derivatives in an extended release formulation providing less than 500mg per dosage form or per daily dose – Sched. II

Since then, Health Canada has revised the proposed regulatory amendment per Project #1508. In order to update the NDSAC Initial Recommendation, the Committee discussed the matter and a motion was brought forward.

It was moved by R. Wilson that the previous Initial Recommendation from September 2005 be replaced with the following: that “nicotinic acid, when sold in a modified-release oral dosage form providing less than 500mg per dosage unit or per daily dose” be placed in Schedule II and that “nicotinic acid when sold in an immediate-release oral dosage form providing 500 mg or less per dosage unit or per daily dose” be Unscheduled (pending federal regulatory changes).

The motion was carried.

It was noted that the above Initial Recommendation is largely administrative, and interim, as nicotinic acid qualifies for regulation as an NHP.

18.0 TPD Amendment Proposals: Proposed Changes to the Food and Drug Regulations

The Committee discussed Health Canada's Project #743 – Non-medicinal Ingredients. Some concern was expressed that including additional information on the labels may reduce the font size and make the information on the active medicinal ingredient less legible.

19.0 TPD Schedule F Amendments: Finalized Changes to Part II of Schedule F

NDSAC was informed that the regulatory amendment proposal for clobetasone butyrate 0.05% cream had been finalized by the federal government, published in Canada Gazette II, and that the NDS changes had been implemented.

20.0 Other Business

M. Priddle asked that time be set aside at a future meeting to discuss issues regarding package inserts.

21.0 Date of Next Meeting

The next NDSAC meeting is scheduled for March 4-5, 2007.

22.0 Closing Comments and Adjournment

The Chair thanked the Members, Observers, and staff for their active participation. The meeting was adjourned at 2:00 pm.

Recorder: Ken Potvin