

Minutes of the National Drug Scheduling Advisory Committee Meeting June 11-12, 2006

A meeting of the National Drug Scheduling Advisory Committee (NDSAC) was held on Sunday and Monday, June 11/12, 2006 at the Lord Elgin Hotel, 100 Elgin St., Ottawa.

Participants:

NDSAC Members: Dr. Jeff Taylor (Chair), Phil Hudson, Dr. Sheldon Koven, Dr. Larry Lynd, Margot Priddle, Dr. Ruth Wilson

Observers: Micheline Ho, Joan Sayer

Staff: Norma Lynn Pearson (Drug Information Specialist, Ottawa Valley Regional Drug Information Service), Ken Potvin (Executive Director, NAPRA)

Regrets: Dawn Frail

Guests: **Pfizer Consumer Healthcare:** Praveen Chawla (Director, Regulatory Affairs), Philloza Suleman (Regulatory Affairs Scientist), Dr. Iris Greenwald (Family Physician)

Sunday June 11, 2006

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

Dr. Taylor called the meeting to order at 9:00 am on Sunday June 11, 2006 and introduced the new physician members, Dr. Sheldon Koven and Dr. Ruth Wilson.

1.1 Conflict of Interest Declarations

Dr. Taylor called for Committee members to declare any real or perceived conflicts of interest. Dr. Lynd reported that Pfizer has committed to providing him with a 'grant in aid' for the study of NSAIDS and Cox-2 Inhibitors. In the interest of ensuring that there was no perceived conflict of interest, Dr. Lynd agreed to exclude himself from deliberations and voting on the drug scheduling reviews submitted by Pfizer for this meeting.

2.0 Approval of the Agenda

On a motion by P. Hudson, the Agenda was approved as circulated.

3.0 Approval of the Minutes of the March 2006 NDSAC Meeting

It was noted that the Minutes from the March 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 Business from Previous Meetings

4.1 Committee Membership

K. Potvin reported that the following membership changes had occurred since the last NDSAC meeting:

- Dr. Sheldon Koven has replaced Dr. Mark Armstrong
- Dr. Ruth Wilson has replaced Dr. Marilyn Caughlin
- Fred Rumpel has resigned and an industry replacement has been appointed by NAPRA's Executive Committee (EC), subject to acceptance by the nominee
- Dr. Jeff Taylor has completed his second three-year term, and a replacement from academia is currently being sought

4.2 Drug Scheduling Decision on Ephedrine/Pseudoephedrine

K. Potvin provided a status update on the provincial/territorial implementation of the recommendations from NDSAC on the changes to the National Drug Schedules (NDS) for ephedrine and pseudoephedrine. J. Sayer circulated a copy of a consumer article on this topic.

4.3 "Schedule F Recommended"

K. Potvin noted that the "Schedule F Recommended" policy was approved by the NAPRA Board at the April 23, 2006 meeting. The medicinal ingredients for which an official regulatory amendment has been commenced, or for which NAPRA has received notice of their "Schedule F Recommended" status from Health Canada, have all been added to the NDS Schedule I as of June 1, 2006. A notice to this effect has been provided to the pharmacy regulatory authorities (PRAs) and the Drug Scheduling External Liaison Group (DSELG), and a News Release was issued on June 8. An article is being prepared for trade publications, and the Canadian Pharmacists Journal.

4.4 Definition of "Marketed"

The revised definition for "marketed", per the input of NAPRA's legal counsel and the approval of NAPRA's EC, was presented to NDSAC. It was agreed that this definition should be posted for external stakeholder consultation (including DSELG, the Pharmaceutical Advertising Advisory Board, and the Advertising Standards Council). The format will be slightly modified, to include bullet points rather than paragraph form.

4.5 NAPRA Board Decision Regarding NHPs

K. Potvin reported that the Directors General of both the Therapeutic Products Directorate (TPD) and the Natural Health Products Directorate (NHPD) had received a letter from NAPRA regarding the Board's decision that Natural Health Products (NHPs) are outside of the scope of the NDS and that NAPRA had some concerns about how Health Canada would ensure public safety in the use of NHPs. No response has been received to date. Mr. Potvin elaborated on some of the background and rationale for the Board's decision. There was subsequent discussion about the proposed OTC amendment to the NHP Regulations and the proposed changes to allow for the advertising of nonprescription products for conditions listed in Schedule A to the Food and Drugs Act.

4.6 NAPRA Policy #9604: Expense Reimbursement & Honoraria for NDSAC Members/Observers

The Committee was informed that NAPRA's Board had recently approved the revised *Policy #9604: Expense Reimbursement & Honoraria for NDSAC Members/Observers*. The matter of reimbursement for travel days was taken under advisement by NAPRA's Board and will be considered in future revisions.

5.0 New Business

5.1 Format Options for Drug Scheduling Review Submissions – Survey Results

K. Potvin thanked those who had participated in the survey, and provided the results for discussion. NDSAC members agreed with the recommendation that the NAPRA office encourages the submission of drug scheduling review applications in electronic format, while continuing to accept paper submissions. The electronic versions would be posted on the restricted NDSAC Members-Only Section of the NAPRA website. If there is a request for a paper copy, NAPRA staff will generate it and provide it to the requesting NDSAC Member/Observer.

5.2 Request for Change to Scheduling Status from Schedule II to Schedule III for:

- **Polymyxin B and its salts and derivatives** (for ophthalmic use)
- **Gramicidin and its salts and derivatives** (for ophthalmic use)
- **Bacitracin and its salts and derivatives** (for ophthalmic use)
- **Lidocaine and its salts** (for otic use)

Pfizer Consumer Healthcare representatives made two presentations, separating the ophthalmic products from the otic preparation, in support of their request to move the above medicinal ingredients from Schedule II to Schedule III. They provided specific arguments against the application of the Scheduling Factors that had been previously assigned, at a time when mass changes were made to the National Drug Schedules.

It was noted that all of these ingredients have Unscheduled status in products for topical application. Revised proposed package labeling, with package inserts, was the basis for much

of the Committee's discussion with Pfizer representatives and the Committee's subsequent deliberations on the scheduling review. While there were some changes required in the proposed labeling (e.g. dosing consistency, ensuring required information such as paediatric precautions are on the external label, highlighting the recommendation to consult a physician if the treatment is ineffective), the Committee agreed that improved labeling would be an important requirement in helping to ensure safe use of these products if they were to be made available without pharmacist involvement as a condition of sale. Pfizer offered to extend to NDSAC Members an opportunity to review the proposed labeling and provide their expert advice prior to finalization. The implications of delayed diagnoses and/or misdiagnoses were thoroughly examined. The lack of reports of serious toxicity, and likelihood that patients would seek professional advice if the therapies were not effective, supported the request for increased access. There was considerable debate about the potential ototoxicity of lidocaine, if used in the presence of a ruptured tympanic membrane. The role of pharmacists in being able to identify such situations came into serious question, although it was acknowledged they would be in a position to highlight such precautions for patients.

The Committee acknowledged that it has a very limited capacity to ensure that labeling is consistent with their expectations in terms of scheduling status assignment, as it is Health Canada's role to approve the labeling of products. NDSAC also makes scheduling decisions on medicinal ingredients, and different manufacturers may well have different labeling. It was agreed that efforts should be made to increase the communication between NAPRA and Health Canada on the labeling of nonprescription products. This will be put on a forthcoming NDSAC meeting agenda, to better understand what NDSAC's role might be in the labeling review and approval process.

After lengthy discussion and deliberation, the Committee agreed that the following scheduling factors were applicable to the ophthalmic medicinal ingredients (polymyxin B and its salts and derivatives; gramicidin and its salts and derivatives; bacitracin and its salts and derivatives): Schedule I - Factor #7, Schedule II - Factor #6 and Schedule III - Factors #1, #2, and #5. For lidocaine and its salts for otic use, the applicable scheduling factors were deemed to be: Schedule III – Factors #1, #2, #5 and #6.

It was moved by R. Wilson that "Polymyxin B and its salts and derivatives (for ophthalmic use)" be moved to Schedule III. The motion was carried.

It was moved by S. Koven that "Gramicidin and its salts and derivatives (for ophthalmic use)" be moved to Schedule III. The motion was carried.

It was moved by M. Priddle that "Bacitracin and its salts and derivatives (for ophthalmic use)" be moved to Schedule III. The motion was carried.

The Committee suggested that the Canadian Ophthalmological Society and the Canadian Examiners in Optometry be advised of these Initial Recommendations.

N.L. Pearson provided a brief synopsis of the quick literature search she had conducted on the ototoxicity of lidocaine, for which the mechanism is unknown. Most of information on this topic is from animal studies. According to some sources, the use of lidocaine is contraindicated for instillation in the middle ear or if it will penetrate the tympanic membrane.

It was noted that systemic lidocaine has also been used to treat tinnitus. A number of other risk factors for ototoxicity were also cited, including the use of other ototoxic meds, prolonged administration, liver dysfunction, elderly, dehydration, and hypersensitivity to the agent.

It was moved by S. Koven that "Lidocaine and its salts (for otic use)" be moved to Schedule III. The motion was carried.

All of the above motions were made with the understanding that product labeling would be improved as per the draft changes from Pfizer Consumer Healthcare (which require further revision, and on which NDSAC members will be provided an opportunity to comment).

It was noted that this would then leave a modified listing for:

Lidocaine and its salts (for ophthalmic or parenteral use, or topical use on mucous membranes, except lozenges) as Schedule II.

The Committee adjourned for the day at 4:10 pm on Sunday June 11.

Monday June 12, 2006

Chair J. Taylor called the meeting to order at 9:05 am on Monday June 12, 2006.

5.3 Review/Pilot of Proposed Revised Scheduling Factors

The Committee spent considerable time reviewing and revising the Proposed Revised Scheduling Factors that had arisen from the discussions at the last NDSAC meeting. A working document is being maintained on this initiative. At the end of the review process, the drug scheduling review requests for this meeting were reconsidered in the context of the proposed scheduling factors (as a pilot initiative). The Committee will continue to pilot the revised factors, incorporating edits as needed, over the course of the next two meetings. The revised factors will then be sent to NAPRA for review and endorsement, followed by an external consultation process.

5.4 Content of Submissions – Consideration of CIOMS Criteria

L. Lynd provided some background on this agenda item, prompted by some concerns about the quality and completeness of some of the drug review submissions NDSAC has received. The intent is to try to improve the quality of the submissions, and change the focus to more of a benefit-risk balance assessment. A checklist to accompany the submission requirements was suggested. As Dr. Lynd had not edited the document obtained from the Council for International Organizations of Medical Sciences (CIOMS), it was being provided to the Committee for information and intended to be used as a starting point for any NDSAC work in this direction. There was some discussion about whether NDSAC should expand its focus on the efficacy of products, as exposure to pharmaceuticals that are not efficacious is not in the best interest of patients. It was noted that Health Canada evaluates products based on

comparative studies, and doesn't specify the proportion of the Canadian population that is likely to benefit from the use of the products. There is also concern among the Committee members that when Health Canada approves new indications for products, there is not then a process whereby the medicinal ingredients are further reviewed by NDSAC for the appropriateness of their scheduling status. NDSAC Members were encouraged to submit comments on the document to L. Lynd, who will then provide a draft specific to NDSAC for the next meeting.

5.5 NAPRA Board Decision on CWHN Request for Review of ECP

K. Potvin informed the Committee about the correspondence that had been exchanged between the Canadian Women's Health Network (CHWN), on behalf of a consortium of organizations, and NAPRA in regard to the schedule status of *levonorgestrel (when sold in concentrations of 0.75mg per oral dosage unit, packaged and labeled for emergency contraception)*.

J. Sayer noted that the advertising and marketing of Plan B is becoming more prominent in the public media.

5.6 TPD Schedule F Amendment Proposal – quinine and its salts and derivatives (Project #1431)

For information only. *Quinine and its salts and derivatives* has been added to Schedule I of the NDS, pursuant to the implementation of NAPRA's Policy for "Schedule F Recommended" Drugs.

5.7 TPD Schedule F Amendment Proposal – agalsidase alfa; botulinum toxin, Type B; laronidase; miglustat; muromo+nab-CD3; pegfilgrastim; pemetrexed and its salts; rasburicase; teriparatide and its salts; vardenafil and its salts (Project #1434)

For information only. These medicinal ingredients have been added to Schedule I of the NDS, pursuant to the implementation of NAPRA's Policy for "Schedule F Recommended" Drugs.

5.8 TPD Schedule F Amendment Proposal – alemtuzumab; azelaic acid; bevacizumab; cetuximab; darifenacin and its salts; efalizumab; emtricitabine; nitric oxide; palifermin; pegvisomant; tipranavir and its salts (Project #1481)

For information only. These medicinal ingredients have been added to Schedule I of the NDS, pursuant to the implementation of NAPRA's Policy for "Schedule F Recommended" Drugs.

6.0 Other Business

There was no other business raised for discussion or information.

7.0 Date of Next Meeting

The next meeting of NDSAC will take place on Sept 17/18, 2006 (to be confirmed after the submission deadline date of July 19).

8.0 Closing Comments and Adjournment

J. Taylor expressed appreciation for the participation of the attendees, on behalf of NAPRA.

The meeting was adjourned at 12:00 pm Monday June 12.

Recorder: Ken Potvin