

Minutes of the National Drug Scheduling Advisory Committee Meeting March 4, 2007

A meeting of the National Drug Scheduling Advisory Committee (NDSAC) was held on Sunday March 4, 2007 at the Hotel Indigo at 123 Metcalfe St in Ottawa.

Participants:

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

Observers: Micheline Ho, Joan Sayer, Karen Wolfe

Staff: Ken Potvin (Executive Director, NAPRA)

Regrets: Phil Hudson, Norma Lynn Pearson

Guests: **sanofi-aventis Canada Inc.:** Katharine Manson (Scientific & Regulatory consultant), Mirela Baranci (Medical advisor), Franca Mancino (Director Regulatory Affairs & Pharmacovigilance)

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

Vice-Chair D. Frail chaired this meeting, as M. Priddle was participating via teleconference. The meeting was called to order at 9:00 am and those participating introduced themselves. Micheline Ho noted that she is planning to retire in the spring of 2007, and that she will seek a replacement representative from within the Therapeutic Products Directorate (TPD). NDSAC Members spoke highly of Ms. Ho's contributions to the work of the Committee over several years, and expressed their appreciation for the unique knowledge and insights she had consistently brought to the table.

1.1 Conflict of Interest Declarations

The Chair called for Committee members to declare any real or perceived conflicts of interest. There were no issues raised in that regard for this particular meeting.

2.0 Approval of the Agenda

On a motion by R. Wilson, the Agenda was approved as drafted.

3.0 Approval of the Minutes of the December 2006 NDSAC Meeting

It was noted that the Minutes from the December 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. K. Potvin reported that the letter regarding Natural Health Products (NHPs) and the National Drug Schedules (NDS), for use by the Pharmacy Regulatory Authorities (PRAs), was near completion and will be distributed shortly.

4.0 Format Options for Drug Scheduling Review Submissions

The Committee confirmed that the current approach to receiving the sponsors' submissions was working well. NAPRA will modify its requirements to state that two hard copies and three CDs are required, with the latter including an editable file of the main submission in MS Word format.

5.0 Content of Submissions

L. Lynd opened up the discussion on the document that he had authored, with input from several Committee members, entitled *Guidelines for Schedule Status Submission for Review by the NDSAC Draft 1*. He noted that this document included integration of materials from CIOMS and NAPRA, and that it was in an early stage of development. There was strong support from the Members to pursue this initiative, with general agreement that, in addition to risk assessment (including sections on toxicity and overdose), professional standards of practice for pharmacists be considered in terms of guiding sponsors in the preparation of their submissions. Suggestions from the meeting participants included separating the document into two parts: an informational piece, and a more succinct guidance document for sponsors. Questions were raised about whether there is a difference in the informational requirements for existing versus newly deregulated medications, and whether the request for information might exceed the capacity of either the sponsor or the Committee. Formatting suggestions, including the development of a template and checklist, were taken under advisement.

It was agreed that L. Lynd would incorporate content revisions as suggested by NDSAC, and in particular by N. MacDonald, after which he would enlist the support of NAPRA office staff to format and refine the document for the next NDSAC meeting.

6.0 Preparation for Drug Scheduling Review Submissions

The participants did not raise any matters for discussion in advance of the sponsor's presentation.

7.0 Request for Change from Schedule III to U for Fexofenadine HCl

Representatives from sanofi-aventis Canada Inc. made a presentation to the Committee to support their request to have *fexofenadine HCl* moved from Schedule III to Unscheduled status. The rationale focused on the favourable profile of this medication as compared with other non-sedating antihistamines. During discussion with the representatives, the prospect of separating the NDS listing for this medicinal ingredient into two – one for adult use and one for paediatric use, was supported in principle.

In the NDSAC deliberations following the formal presentation and discussion, it was noted that although there are no paediatric formulations on the market at the present time, the Committee should consider that possibility in its decision. The Committee also had a lengthy discussion about the indications for the various products with this medicinal ingredient. While the 12-hour formulation is approved for relief of symptoms in seasonal allergic rhinitis (SAR), perennial allergic

rhinitis, and chronic idiopathic urticaria, the 24-hour product is only approved for SAR symptoms. While the submission and presentation from the sponsor focused on the use of the medication in SAR, NDSAC members concluded that imposing restrictions based on that specific indication was not warranted.

The Committee agreed that the following scheduling factors were applicable to this medicinal ingredient: Schedule III – Factors #1, #3, and #4. These factors were not considered sufficient for the Committee to retain the products, marketed for adult use, in Schedule III.

It was moved by S. Koven that “fexofenadine HCl (in products marketed for adult use – 12 years and older)” be moved to Unscheduled status and that “fexofenadine HCl (in products marketed for paediatric use – under 12 years of age)” be retained in Schedule III.

The motion was carried.

8.0 Reassessment of Diphenhydramine

The Committee had extensive discussion on the sponsor’s request for a revised drug schedule listing review for certain diphenhydramine products. It was acknowledged that the company had made substantive effort to address some of the concerns raised in NAPRA’s response regarding the review conducted at the December 2006 NDSAC meeting. The Committee had lingering concerns however, about adverse effects of this medication, particularly in the elderly population. These concerns had not been alleviated, in the original submission nor in the ensuing correspondence.

The Committee reviewed the scheduling factors again, with a focus on oral single ingredient diphenhydramine products marketed for the treatment of allergies in adults. It was agreed that the following scheduling factors were applicable to this medicinal ingredient in that context: Schedule III – Factors #1, #3, #4, #6 and #8. These factors were considered sufficient for the Committee to deny the request and to retain the current schedule status of oral diphenhydramine.

It was moved by S. Koven that the schedule status of “Diphenhydramine and its salts and preparations (except for parenteral or topical use)” remain in Schedule III.

The motion was carried.

9.0 Schedule Status of Loperamide Oral Liquid for Adults

The Committee discussed the request from McNeil Consumer Healthcare to make an administrative change to the NDS, in order to clarify the status of *loperamide and its salts in an oral liquid dosage form marketed for adult use*. The current listings do not contemplate such products.

NDSAC Members discussed the relative significance of liquid formulations, versus the importance of addressing concerns about the use of this medication in paediatric populations regardless of the dosage form. There was general agreement that revisions to the NDS listings would be appropriate, to recognize these concerns and to address the request for clarification from the company.

It was moved by R. Wilson that the following NDS amendments be made: “Loperamide and its salts in products marketed for adult use – 12 years and older” - Unscheduled; and “Loperamide and its salts in products marketed for paediatric use – under 12 years of age” – Schedule II.”

The motion was carried.

10.0 Review/Pilot of Proposed Revised Scheduling Factors

The Committee undertook a final exercise of piloting the revised version of the scheduling factors, using the fexofenadine submission. In doing so, it was found that the resulting schedule status recommendation would not have been any different using the revised factors, and that there were only minor wording amendments to make for clarity.

The latest version will be submitted as a recommendation to NAPRA’s Executive Committee, after which external public consultation is anticipated.

11.0 Package Inserts

NDSAC discussed several issues regarding package labeling and product inserts, noting in particular that warnings may not be sufficient in terms of availability or readability prior to consumers’ purchases. M. Ho provided the Committee with information on Health Canada’s current requirements, and described the process for proposing any amendments to existing Regulations. It became clear in the discussion that this is a complex matter, and that establishing more specific labeling standards would require expertise and support that extends beyond NDSAC/NAPRA. The Canadian Standards Association was cited as an organization that had contributed to the development of current labeling standards for injectable products. No specific action was committed to at this time.

12.0 Other

12.1 Update from TPD

M.Ho provided information items of interest to NDSAC:

- Omer Boudreau, former Director General (DG) at the TPD, has recently left the Directorate and Dr. Supriya Sharma is now the Acting DG.
- A new version of the Labeling Guidelines document is undergoing internal review, and this will be followed by external consultation. NAPRA will monitor the release of the revised document, and afford NDSAC an opportunity for input.
- The posting of Product Monographs remains under discussion at TPD, with unresolved issues such as when and where to release and post them electronically.
- There are new documents posted on the Health Canada website entitled *Summary Basis of Decisions*, which are currently available only for new chemical entities. These may be useful to the Committee, and NDSAC should let the Branch know what would be helpful for inclusion in this type of report, for example in terms of considering Rx-OTC switches.

12.2 Drug Listing Inquiries

K. Potvin noted that he had a considerable amount of discussion recently with Health Canada staff about the rationale and implications for Vitamin A being listed in Part II of Schedule F. Apparently this was done on the advice of legal counsel and the Part I listing should guide the regulatory requirements for human use. He also noted that the NDS listings for hydrocortisone topical products were recently revised to be consistent with the Schedule F descriptions (i.e. “0.5%”, rather than “0.5% or less”). This is a temporary measure, as the products in question will imminently be regulated as NHPs. M. Ho noted that there is currently a consultation process underway regarding the NHP Regulations.

13.0 Date of Next Meeting

The next NDSAC meeting is scheduled for June 10-11, 2007, subject to the receipt of a submission by the April 11th deadline.

14.0 Closing Comments and Adjournment

D. Frail thanked the participants for their hard work, and expressed sincere appreciation for the exceptional contributions of M. Ho and K. Potvin over the past several years, both of whom were attending their last NDSAC meeting.

The meeting was adjourned at 3:35 pm.

Recorder: Ken Potvin