

A meeting of the National Drug Scheduling Advisory Committee (NDSAC) was held on Monday, December 5, 2016 at the Lord Elgin Hotel, Ottawa.

Present:

NDSAC members:

Dr. Tom Bailey (Chair), Dr. Murray Brown, Ms. Drena Dunford; Dr. Melanie Johnson, Dr. Deborah Kelly, Dr. Jason Kielly, Ms. Judy McPhee

Observers:

Dr. Ratna Bose – Natural and Non-prescription Health Products Directorate, Health Canada
Ms. Joan Sayer – Consumers Association of Canada

NAPRA Staff:

Ms. Adele Fifield – Executive Director
Dr. Sarah Jennings – Acting Manager, Professional and Regulatory Affairs; Committee Secretary

Regrets:

Ms. Kendra Townsend (Vice Chair)

1.0 Call to order

1.1 Opening remarks

T. Bailey welcomed everyone and called the meeting to order at 9:08 a.m. (ET) on December 5, 2016.

1.2 Conflict of interest declarations

T. Bailey called for conflict of interest declarations. Dr. Brown reported that he recently served as a consultant for Adapt Pharma. This company is new to the Canadian market and sought Dr. Brown's advice in navigating Canadian regulatory systems. It was agreed that this may represent a conflict of interest. Therefore, it was agreed that Dr. Brown would abstain from the votes related to naloxone nasal spray.

Members were also asked to sign and submit their written conflict of interest declarations, which are collected annually.

2.0 Approval of the agenda

The agenda was approved with the addition of a Health Canada update from R. Bose.

3.0 Approval of minutes

3.1 Approval of the minutes from the June 6, 2016 meeting

A motion to approve the minutes from the NDSAC meeting of June 6, 2016 as posted on the NAPRA website was put forward by M. Brown, seconded by D. Dunford and approved by consensus.

4.0 New Business

4.1 Request for Schedule II status for naloxone hydrochloride nasal spray, when indicated for emergency use for opioid overdose outside hospital settings.

The committee reviewed and considered the application for drug scheduling. One request for interested party status was received after the deadline. This submission was provided to the committee via the alternate method of participation.

At 10:15 a.m., T. Bailey welcomed representatives from Adapt Pharma Canada Ltd: David Renwick, General Manager, Adapt Pharma Canada Ltd; Joyce Reyes, Consultant; John Wong, Consultant. The Adapt Pharma representatives gave a short slide presentation to the committee, which was followed by a question and answer period.

The committee then discussed the information previously provided to them for review and consideration, as well as the information received during the company presentation and the subsequent question and answer period.

The committee discussed the need for user training. As with injectable naloxone, it is crucial that bystanders call for medical assistance and understand the potential for rebound toxicity. In particular, it was noted that the media attention around this drug has positioned it as “life-saving,” without necessarily highlighting the adjunctive therapy and follow-up that are required. The committee encouraged the manufacturer in their plan to create a consumer-focused website tailored to the Canadian market.

The committee recognized the safety of naloxone. The drug has virtually no pharmacological activity in opioid-naïve persons, and a low risk of adverse effects or misuse. The committee recognized that acute opioid withdrawal syndrome (AOWS) can occur and that it is usually non-fatal, but they noted the seriousness of AOWS in a neonate or pregnant woman. It was agreed that the likelihood of administration of naloxone to a neonate outside of hospital is very low. The committee also recognized the use of naloxone in “flat-lining,” but concluded that in this case the benefits of increased access for all outweighed the risks of illicit misuse by some.

The committee discussed the intranasal formulation and new drug delivery device. The manufacturer conducted consumer usage studies showing that most bystanders could administer the product correctly without training. However, some participants made errors such as administering the drug into the mouth rather than the nose, or testing the device and thereby losing the dose. The plunger on the device cannot be depressed a second time, so it should be clear to the user that the dose has been lost. As well, the inner labelling (blister pack) says, “Do not test the spray device.” However, the committee suggested that this statement be made more prominent. The committee also encouraged the manufacturer to distribute demonstrator devices more broadly.

The committee recognized that the new drug delivery device has been available in Canada since June 2016, under the terms of an Interim Order issued by the federal Minister of Health. However, 85% of all doses imported under the Interim Order have been purchased by law enforcement groups, and therefore the committee did not consider there to be widespread usage and familiarity with the product at this point in time.

The committee discussed some of the societal issues surrounding access to naloxone, with the recognition that NDSAC's Scheduling Factors focus on efficacy and safety of drugs rather than other issues such as ethical, legal, or social implications (ELSI). It was recognized that the public need for the drug seems to be urgent, with a great deal of political pressure for increased access. It was also recognized that drug scheduling is not the only factor involved in increasing access. For example, the committee discussed the cost of the product as compared to the injectable, questions around reimbursement, and the challenges in stocking the product, such as monitoring expiry dates and placing the product so as to discourage theft.

T. Bailey led the group in a review of the applicability of the National Drug Scheduling Factors. It was agreed that the following scheduling factors were applicable to naloxone hydrochloride nasal spray:

- #I-2, II-3, II-9, II-10, III-2, III-5

There was an initial lack of consensus on factor #II-6 and there was significant discussion. The committee agreed that there is value in pharmacist intervention, including reminders to call 911 and instruction on recognizing rebound toxicity. Ultimately, a slight majority of members felt that pharmacist intervention was not strictly required prior to selection of the drug, therefore this factor was deemed non-applicable.

The committee discussed the overall best fit for the scheduling of this substance. Injectable naloxone was granted Schedule II status in June 2016, and it was agreed that naloxone nasal spray is safer and easier for bystanders to administer. The committee also discussed whether the need for pharmacist intervention may be perceived as a barrier to access in some communities. Conversely, the committee agreed that the drug is still relatively new to the non-prescription market, this formulation is a new drug delivery system, and consumers would benefit from education at the point of purchase. Such education could include recognizing the signs and symptoms of opioid overdose, reminders to call 911, instruction on recognizing rebound toxicity and giving repeat doses, monitoring the expiry date of the product, and emphasizing the importance of not testing or priming the device as the dose would then be lost; the committee felt that the product labelling could be clearer on this last point. Finally, it was noted that Schedule II status would not be a barrier for public health, first responders, correctional officers, and other outreach workers to access the product. It was agreed that the best placement for this drug would be Schedule II.

MOTION: It was moved by D. Kelly, seconded by D. Dunford to recommend that: **naloxone hydrochloride nasal spray, when indicated for emergency use for opioid overdose outside hospital settings, be granted Schedule II status.**

Motion carried. M. Brown abstained.

This recommendation will be reported to the NAPRA Executive Committee.

5.0 Advice to NAPRA regarding submission guidelines

The committee discussed drug scheduling submissions from interested parties. Bylaw No. 2 allows for this. However, when the scheduling request is pursuant to a

deregulatory proposal, submission instructions state that the applicant must provide NDSAC with the report prepared by the Therapeutic Products Directorate (TPD) panel of reviewers. This report is only available to the manufacturer who submitted the deregulatory proposal to Health Canada, and therefore interested parties would be unable to prepare a complete NDSAC submission.

The committee agreed that interested parties should make every effort to provide the information. Options include requesting a redacted version of the TPD report via an Access to Information (ATI) request, and conducting a thorough literature search to find publicly-available data on clinical efficacy and safety. If the interested party is a manufacturer that markets the same molecule but did not submit the deregulatory proposal, they should submit the documentation used to attain their Notice of Compliance (e.g., bioequivalence studies).

6.0 Updates

6.1 Natural and Non-prescription Health Products Directorate

Dr. R. Bose provided an update on the Self-Care Framework work that is currently ongoing. She also provided an update on the acetaminophen labelling standard that is now a final guidance document. She also shared information on the guidance document on the Drug Facts Table, which includes Facts Tables for about 150 medicinal ingredients that are currently present in non-prescription drugs marketed in Canada, and, has been drafted using the standardized format as described in the Good Label and Package Practices Guide for Non-prescription Drugs and Natural Health Products (June 30, 2016). Regulatory requirements with respect to the Plain Language Labelling that will be coming into force on June 13, 2017 for non-prescription drugs were also discussed.

7.0 Next meeting

Tentatively set for March 19-20, 2017.

8.0 Adjournment

The meeting was adjourned at 1:30 p.m.