

A virtual meeting of the National Drug Scheduling Advisory Committee (NDSAC) was held on Monday, June 15, 2020 and Thursday, June 18, 2020.

Present:

NDSAC members:

Dr. Deborah Kelly (Chair); Dr. Murray Brown; Dr. Drena Dunford; Dr. Melanie Johnson; Dr. Jason Kielly; Mr. Kevin Pothier; Ms. Kendra Townsend

Observers:

Ms. Joan Sayer – Consumers Association of Canada

Dr. Shiva Ghimire - Natural and Non-prescription Health Products Directorate, Health Canada

NAPRA Staff:

Sarah Marshall – Manager, Professional and Regulatory Affairs, Committee Secretary

Elizabeth Kozyra - Pharmacy Practice Specialist

Sarah ter Huurne - Pharmacy Practice Advisor

Lisa Shaver - Standards and Competencies Specialist

1.0 Call to order

1.1 Opening remarks

D. Kelly welcomed everyone and called the meeting to order at 11:00 a.m. (ET) on Monday, June 15, 2020. The meeting ended at 5:26 p.m. (ET) on June 15, 2020 and resumed again at 2:02 p.m. (ET) on June 18, 2020.

1.2 Roll call and declaration of quorum

D. Kelly noted the members in attendance and declared quorum.

1.3 Welcoming new member

D. Kelly welcomed Mr. Kevin Pothier as a new member of the NDSAC.

1.4 Conflict of interest declarations

D. Kelly called for conflict of interest declarations. None of the members had any conflicts of interest to declare.

2.0 Approval of the agenda

A motion to approve the agenda as presented was put forward by D. Dunford, seconded by K. Townsend and approved by consensus.

3.0 Confirmation of approval of the minutes from the December 1, 2019 NDSAC meeting

The minutes of this meeting had previously been approved by the NDSAC members via email. A motion to formally confirm approval of the minutes from the NDSAC meeting of December 1, 2019 as posted on the NAPRA website was put forward by M. Johnson, seconded by J. Kielly, and approved by consensus.

4.0 New Business

4.1 Request for Schedule II status for fixed-dose combinations of acetaminophen and ibuprofen

The committee reviewed and considered the application for drug scheduling, as well as additional information submitted through the Interested Party process and the Alternate Method of Participation. Glaxo Smith Kline Consumer Healthcare Inc., Bayer Inc. Consumer Health, and Consumer Health Products Canada were granted interested party status. Thirteen interrogatories were completed during the interrogatory process. There were two submissions of information by interested parties. The committee received two submissions via the alternate method of participation.

At 11:45 a.m., D. Kelly welcomed representatives from Glaxo Smith Kline Consumer Healthcare (GSK): Ms. Amanda Wong, Ms. Anjali Newman, and Dr. Mahsa Jafari. The GSK representatives gave a concise slide presentation to the committee, which was followed by a question and answer period.

At 12:50 p.m., D. Kelly welcomed representatives from Consumer Health Products Canada (CHP Canada): Mr. Gerry Harrington and Ms. Kristin Willemsen. The CHP Canada representatives gave a concise slide presentation to the committee, which was followed by a question and answer period.

At 2:00 p.m., D. Kelly welcomed representatives from BioSyent Pharma Inc: Dr. Navid Ashrafi, Ms. Susanne Picard, and Mr. Joost van der Mark. The BioSyent Pharma representatives gave a concise slide presentation to the committee, which was followed by a question and answer period.

The committee then discussed all of the information previously provided to them for review and consideration, as well as the information received during each of the presentations and the subsequent question and answer periods.

Members were concerned about the potential risks to consumers, particularly from long-term use. Serious adverse effects and drug interactions can occur with ibuprofen and acetaminophen. For example, ibuprofen may increase the risk of cardiovascular events, renal toxicity and gastrointestinal toxicity including stomach bleeding. Acetaminophen may cause liver toxicity, especially in overdose. Both drugs can cause serious drug interactions, for example both drugs interact with warfarin, as well as many other medications. Although serious adverse effects and interactions with ibuprofen and acetaminophen are uncommon at the non-prescription dose and duration of use, the risks have been shown to augment with increased dose and duration of use and it is known from experience and from the literature that consumers do use non-prescription acetaminophen and ibuprofen off-label on a long-term basis. Clinical trials and global safety data to date show that fixed-dose combinations (FDCs) of acetaminophen and ibuprofen do not appear to lead to a greater risk of adverse effects and drug interactions at the non-prescription dose and duration of use. However, there is limited evidence about the long-term safety of FDCs of acetaminophen and ibuprofen. Further, although

taking a FDC of acetaminophen and ibuprofen for the non-prescription duration of use of 3-5 days is not expected to significantly delay recognition or mask the symptoms of serious disease, longer treatment could potentially cause issues in this regard. Therefore, the committee concluded that assessment and monitoring of consumers using FDCs of acetaminophen and ibuprofen long-term is required to assess these individuals for potentially serious underlying conditions, determine whether continued treatment is appropriate and determine whether further intervention of a health professional is required, given the serious adverse effects and drug interactions that can occur with long-term use.

The committee was also concerned about the quality of the labelling and the label comprehension study presented in the applicant's submission and deliberated on the ability of consumers to understand the labelling without assistance. Members were concerned that the very general statements on the outer label might make it difficult for consumers to identify when the warnings would apply to them and that the overwhelming amount of information on the labels could lead to consumers not reading the label or not finding the information they need. The label comprehension results presented did not address whether consumers could understand when warnings applied to them and there was a signal regarding potential information overload in the label comprehension study presented by the applicant. The committee acknowledged that the risk of serious adverse events as a result of potentially confusing labelling was likely to be low, if used at the approved non-prescription dose and duration of use. The main concerns centered around the risks of acetaminophen overdose and the risks of adverse effects from long-term use of ibuprofen, if the dose and duration of use for the non-prescription setting were not well understood. After discussion, the committee determined that there was enough information in the labelling to at least prompt consumers to speak with a pharmacist to determine whether the general warning statements applied to them or to request clarification if they were having difficulty understanding the labelling, but noted that a pharmacist should be available to help consumers seeking such guidance.

It was agreed that product selection was likely to cause confusion and that a pharmacist should be available to assist consumers in this regard. Because the fixed-dose combination of acetaminophen and ibuprofen is new to Canada, there could be an increased risk of confusion and inadvertent duplication of therapy, which a pharmacist could address. A pharmacist could also assist consumers in determining when the combination product might be appropriate versus single-ingredient therapy. It was acknowledged that the Health Canada approved indications for the FDC of acetaminophen and ibuprofen are not restricted to individuals who have failed monotherapy and that the risks of using the FDC of acetaminophen and ibuprofen when single-ingredient therapy might suffice would be low at the approved dose and duration of use of 3-5 days. However, members agreed that a pharmacist could help to optimize therapy and minimize the risks of combination therapy being used inappropriately long-term, given the above-noted concerns related to long-term use.

D. Kelly 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 fixed-dose combinations of acetaminophen and ibuprofen:

- #I-4, I-6, II-2, II-10, III-1, III-2, III-3, III-5

The committee discussed the overall best fit for the scheduling of FDCs of acetaminophen and ibuprofen. Due to the concerns with the quality of the labelling and label comprehension results, the committee agreed that a pharmacist must be available to assist consumers with product selection and to clarify potentially confusing information in the product labelling. Given that FDCs of acetaminophen and ibuprofen are new in both Canada and the United States, there is a need for post-market data on real-world use in these countries, to ensure that safety signals do not arise from the patterns of use of FDCs of acetaminophen and ibuprofen in North America. There is also a need for more comprehensive and robust label comprehension and actual use studies. The committee therefore agreed that an Unscheduled environment was not appropriate.

Since the greatest potential risks to consumers are the potential for acetaminophen overdose and serious adverse effects from long-term use and given the limited data on the long-term safety of FDCs of acetaminophen and ibuprofen, the committee agreed that package sizes above the maximum duration of use approved for the non-prescription setting should be Schedule II, to help mitigate the potential for overdose or long-term use and ensure the required assessment and monitoring of consumers using the drug long-term.

MOTION: It was moved by K. Townsend, seconded by K. Pothier to recommend that:

Acetaminophen and ibuprofen in oral, fixed-dose combinations, in package sizes containing 20,000 mg or less of acetaminophen and 6,000 mg or less of ibuprofen, be granted Schedule III status and

Acetaminophen and ibuprofen in oral, fixed-dose combinations, in package sizes containing either more than 20,000 mg of acetaminophen or more than 6,000 mg of ibuprofen, be granted Schedule II status

Motion carried. All members agreed to the above noted motion.

This recommendation will be reported to the NAPRA Board of Directors.

It was noted that when the National Drug Schedules are updated, it will be important to clarify via footnote that ibuprofen that is listed on the Prescription Drug List requires a prescription and is excluded from these listings.

5.0 Updates

5.1 NAPRA Strategic Plan 2019-2023

S. Marshall provided an update on progress towards the NAPRA Strategic Plan 2019-2023, including plans to continue moving forward on the review of the NDS program. The project was put on hold while the priorities of NAPRA and its members were focused on the COVID-19 pandemic, but is expected to resume shortly and continue for the next few years.

6.0 Next meeting

Tentatively scheduled for September 27-28, 2020.

7.0 Adjournment

The meeting was adjourned at 4:05 p.m. (ET) on June 18, 2020.