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Health Product InfoWatch

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REPORTING ADVERSE REACTIONS

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This monthly publication is intended primarily for healthcare professionals and includes information on pharmaceuticals, biologics, medical devices and natural health products. It provides a summary of key health product safety information published in the previous month by Health Canada, as well as a selection of new health product safety information meant to raise awareness. New information contained in this issue is not comprehensive but rather represents a selection of clinically relevant items warranting enhanced dissemination.

Canada

MONTHLY RECAP OF HEALTH PRODUCT SAFETY INFORMATION

The following is a list of health product advisories as well as summaries of completed safety reviews published in February 2016 by Health Canada.

Advil liquid products for infants and children Information Update	Pfizer Consumer Healthcare has recalled 126 lots of Advil liquid products for infants and children because of a potential risk of inconsistences in dosing of the product. "Clumps" of ibuprofen may form in the bottle and lead to higher or lower doses that are given to infants and children if it is not shaken well before each use.
Cisplatin Summary Safety Review	This safety review evaluated the potential increased risk of venous thromboembolism with the use of cisplatin. Health Canada's review considers that there is an increased risk of venous thromboembolism with the use of cisplatin in the treatment of advanced bladder, testicular and ovarian cancers. Health Canada has recommended that the prescribing information for cisplatin products be updated by all manufacturers of cisplatin in Canada to include warnings about this increased risk.
Forta for Men Advisory	All lots of the product "Forta for Men" (NPN 80045132) were recalled after Health Canada testing confirmed one lot contained an undeclared drug: tadalafil. The same distributor as "Forta for Men" is also recalling all lots of "Durazest for Men" (NPN 80033381) as a precautionary measure.
Piperacillin/Tazobactam for Injection and Piperacillin for Injection Summary Safety Review Health Product InfoWatch	This safety review evaluated the potential link between drug reaction/rash with eosinophilia and systemic symptoms (DRESS) and the antibiotic drug combination piperacillin and tazobactam or piperacillin alone. Health Canada's review concluded that there is evidence of a link between the drug combination piperacillin and tazobactam and DRESS. Additionally, a contributing role for piperacillin alone and DRESS could not be ruled out. Health Canada has begun updating the Canadian prescribing information to include this risk. Health Canada has also communicated this information to healthcare professionals.
Pseudoephedrine-containing products Summary Safety Review Health Product InfoWatch	This safety review evaluated the potential link between the use of pseudoephedrine and ischemic colitis. Health Canada's review concluded that there is very limited evidence of ischemic colitis linked with the occasional use of pseudoephedrine at recommended dose and duration, in the absence of other risk factors. Health Canada will continue to monitor this issue. Health Canada has also communicated this information to healthcare professionals.

Unauthorized health products labelled as B17/ amygdalin/bitter apricot kernel

Advisory (update)
Advisory

Canadians were advised that a number of potentially dangerous unauthorized health products labelled as B17/ amygdalin/ bitter apricot kernel were available for sale in Canada. No health products containing B17 or amygdalin have been authorized by Health Canada to treat cancer or any other condition.

Did you know?

Health products that have been authorized for sale by Health Canada have an eight-digit Drug Identification Number (DIN), a Natural Product Number (NPN) or a Homeopathic Medicine Number (DIN-HM).

NEW HEALTH PRODUCT SAFETY INFORMATION

The following topics have been selected to raise awareness and, in some cases, to stimulate reporting of similar adverse reactions.

REVIEW ARTICLE

Melatonin and neurologic adverse reactions in children and adolescents

Key points

- In Canada, melatonin is licensed as a natural health product ingredient and is used as a sleep aid.
- Serious neurologic adverse events suspected of being associated with the use of melatonin have been reported in children and adolescents, both in Canada and internationally.
- Based on current evidence, a relationship between the pediatric use of melatonin and the occurrence of neurological adverse reactions such as seizures could not be established.

Melatonin is a hormone that is secreted by the pineal gland in response to darkness.[1] It helps regulate the sleep/wake cycles, and is used for the management of sleep disorders. In Canada, melatonin is designated as a natural health product (NHP) and is indicated for adult use.[2,3] Health Canada has licensed over 500 melatonin-containing NHPs either as single ingredients or multi-ingredient formulations in the form of capsules, sublingual tablets, liquids and gums. In addition, 2 multi-ingredient melatonin cold remedies have been licensed for children 12 years and older since 2011; however they are not currently marketed in Canada. Although little is known about its safety and efficacy in children and adolescents, melatonin has been used in this population, both in Canada and internationally.[4-6]

Recent international reports of neurological adverse reactions (e.g., anxiety, panic reactions, visual hallucinations and seizures) suspected of being associated with the use of melatonin in children and adolescents have been brought to Health Canada's attention by foreign regulators.

A review was conducted on the use of melatonin in the pediatric population.[7] At the time of the review, Health Canada had received 18 Canadian reports of adverse reactions suspected of being associated with the use of melatonin-containing NHPs in children and adolescents. The most

Key points (continued)

- Healthcare professionals are encouraged to report to Health Canada any adverse reactions suspected of being associated with the use of melatonin.

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frequently reported adverse reaction was daytime sleepiness. Of the 18 cases, 5 were considered serious. Two cases occurred in children with an established diagnosis of epilepsy: one child had a seizure, and the other had an increase in seizure frequency while taking melatonin and carbamazepine. Another child who was known to have attention deficit hyperactivity disorder (ADHD) as well as complex psychological problems developed anxiety, a panic reaction and visual hallucinations while taking melatonin and an ADHD medication. The other 2 serious cases described dyspnea and an increase in liver enzymes. In all cases received by Health Canada, information was limited; therefore, a causal association between the use of melatonin and these adverse reactions could not be established.

A review of international data from the World Health Organization's Global Individual Case Safety Reports Database System (VigiBase) identified 163 reports of adverse reactions, including 8 from Canada, suspected of being associated with the use of melatonin in the pediatric population.* The most commonly reported adverse reactions were general fatigue, aggression, abnormal dreams, and headache. Seventy-one of the non-Canadian cases were considered serious, but they could not be assessed further due to limited information available.

Evidence from the scientific literature on the safety and efficacy of melatonin is limited, and suggests that melatonin is only modestly effective in improving sleep quality in adults.[8-10] Some systematic reviews have supported the hypothesis that melatonin decreases sleep onset latency and increases total sleep time in certain patients when used for less than 4 months, though improvements are modest.[9,10] Some studies have also shown potential benefits for certain sleep problems in children.[4,6,11-13] Studies in special populations (e.g., ADHD, autism spectrum disorders) provide the best evidence for the usefulness of melatonin in children.[4,6,11,13] However, child behaviour and family functioning outcomes did not improve consistently.[4,5,12] Adverse reactions reported in these studies, including neurological reactions, appear to be mild or limited with short term use.[4-6,11,13,14] Based on current evidence, a relationship between the pediatric use of melatonin and the occurrence of neurological adverse reactions, such as seizures, could not be established.[5,6,13,14] In addition, the short term impact on psychological development and the long term effect on growth in the pediatric population remain uncertain, and more studies are needed in the future to better characterize these issues.[4,5,11,12,14,15]

Parents and caregivers should be encouraged to speak to a healthcare professional about the risks and benefits of using melatonin products as sleep aids in children. In addition, the use of pharmacological therapy for sleep problems in children and adolescents should only be considered after behavioral interventions.[5,11,14] Sleep hygiene interventions for pediatric sleep problems have been shown to produce clinically significant improvements. Healthcare professionals are encouraged to report to Health Canada any adverse reaction suspected of being associated with the use of melatonin. Information such as the dosage, duration of exposure to melatonin, concomitant medications and time to onset of adverse events are important to include when reporting adverse reactions.

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* World Health Organization (WHO) adverse reaction information provided by: The WHO Collaborating Centre for International Drug Monitoring. This information is not homogeneous with respect to the sources of the information or the likelihood that the health product caused the suspected adverse reaction. Also, this information does not represent the opinion of the WHO.

HELPFUL LINKS

- MedEffect™ Canada
- Recalls and Safety Alerts Database
- Summary Safety Reviews
- New Safety Reviews
- Canada Vigilance Adverse Reaction Online Database
- Drug Product Database
- Medical Devices Active Licence Listing
- Licensed Natural Health Products Database
- The Drug and Health Product Register
- Canadian Drug Shortage Database

Suggestions?

Your comments are important to us. Let us know what you think by reaching us at InfoWatch_InfoVigilance@hc-sc.gc.ca

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Adverse reactions (ARs) to health products are considered to be suspicions, as a definite causal association often cannot be determined. Spontaneous reports of ARs cannot be used to estimate the incidence of ARs because ARs remain underreported and patient exposure is unknown.

Due to time constraints relating to the production of this publication, information published may not reflect the most current information.

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