



# Health Product InfoWatch

April 2017

## HEALTH PRODUCTS MENTIONED IN THIS ISSUE

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### Pharmaceuticals and Biologics

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- Fluorouracil Injection
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### Medical Devices

- Esophageal stents

### Other

- Foreign health products
- Unauthorized health product (PureCare Herbal Cream)
- Unauthorized health products (Botulax and The Lift II)
- Unauthorized health products (EPCA Shipping Inc.)
- Unauthorized health products promoted for sexual enhancement

### REPORTING ADVERSE REACTIONS

Canada Vigilance Program  
 Online: [www.health.gc.ca/medeffect](http://www.health.gc.ca/medeffect)  
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 Fax or mail: Form available online

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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.

## 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 March 2017 by Health Canada.

<b>Buckley's syrups</b> <a href="#">Advisory</a>	Health Canada advised Canadians that GlaxoSmithKline Consumer Healthcare Inc. recalled certain Buckley's syrup products from stores. A defect with the plastic seal may cause it to fall into the bottle and present a potential choking hazard if swallowed.
<b>Esophageal stents</b> <a href="#">Summary Safety Review</a> <a href="#">Health Product InfoWatch</a>	This safety review evaluated and confirmed the risk of esophageal and vascular erosion associated with esophageal stents. Health Canada will work with device manufacturers to update the safety information for all esophageal stents to include details about this potential risk and factors that may increase this risk. Health Canada has also communicated this information to healthcare professionals.
<b>Fluorouracil Injection, BP (5-fluorouracil) 5 g/100 mL</b> <a href="#">Health Product Risk Communication (update)</a>	As an update to the October 2016 risk communication, and in light of the reported shortage for this drug, Health Canada facilitated the release of Fluorouracil vials. The vials had previously been quarantined by the company due to the risk associated with the possibility of cracks or leaks. Vials that show cracks, leakage, or white powder on the outside of the vial should not be used.
<b>Foreign health products</b> <a href="#">Foreign Product Alert (14 products)</a> <a href="#">Foreign Product Alert (16 products)</a>	These foreign health products have been found by regulators in other countries to contain undeclared drug ingredients. The products are not authorized for sale in Canada and have not been found in the Canadian marketplace but it is possible they may have been brought into the country by travellers or purchased over the Internet.
<b>Keytruda (pembrolizumab)</b> <a href="#">Health Product Risk Communication</a>	Cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), some with fatal outcomes, have been reported in patients treated with Keytruda. Healthcare professionals are advised to counsel patients about the benefits and risks of Keytruda; suspend Keytruda treatment and refer for immediate specialized evaluation and treatment if a patient reports any severe skin reaction, or in a case of suspected SJS or TEN; and permanently discontinue Keytruda if SJS or TEN is confirmed. Health Canada is currently working with the manufacturer to include this safety information in the Canadian product monograph.

<p><b>Unauthorized health product (PureCare Herbal Cream)</b></p> <p>Advisory</p>	<p>Health Canada advised Canadians that the unauthorized health product “PureCare Herbal Cream” may pose serious health risks. The product is promoted as a natural treatment for eczema and psoriasis in children and babies. Health Canada testing confirmed the presence of clobetasol propionate and phenoxyethanol not declared on the product label.</p>
<p><b>Unauthorized health products (Botulax and The Lift II)</b></p> <p>Advisory</p>	<p>Health Canada advised Canadians that it seized the unauthorized injectable health product “Botulax” and unauthorized medical sutures “The Lift II” from SPMU-MTS Studio in Richmond, BC. Botulax is labelled to contain botulinum toxin type A and was being administered as an injectable treatment for cosmetic purposes. The Lift II is an absorbable suture used to close incisions after surgery. Neither product is authorized for sale in Canada.</p>
<p><b>Unauthorized health products (EPCA Shipping Inc.)</b></p> <p>Advisory</p>	<p>Health Canada advised Canadians that it seized several unauthorized health products from EPCA Shipping Inc. in Richmond, BC. The products are promoted to treat cancer, infertility, respiratory diseases, enlarged thyroid and erectile dysfunction, and are labelled to contain various prescription drugs.</p>
<p><b>Unauthorized health products promoted for sexual enhancement</b></p> <p>Advisory</p>	<p>Health Canada advised Canadians that it seized multiple unauthorized health products from 3 retailers in Ontario. The products are promoted for sexual enhancement and were found to contain, or are labelled to contain, prescription drugs (dapoxetine, sildenafil, tadalafil and yohimbe).</p>
<p><b>Zydelig (idelalisib)</b></p> <p>Summary Safety Review</p>	<p>This safety review evaluated the risk of serious infections associated with Zydelig (idelalisib). Health Canada’s review concluded that there was a risk of serious infections, which may lead to death, associated with Zydelig use. The Canadian product monograph has been updated to warn about the increased risk of infections. Health Canada has requested the manufacturer to provide any new information on this safety issue.</p>

## 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.

## PRODUCT MONOGRAPH UPDATES

The following safety labelling updates, which were recently made to the Canadian product monograph, have been selected for your awareness. A complete list of safety labelling updates for brand name pharmaceutical drugs is available on [Health Canada's Web site](#).

### Amiodarone (intravenous)

Information regarding **cardiovascular risks** associated with the use of amiodarone **in pediatric populations** has been added to the *Warnings and Precautions* section of the Canadian product monograph for intravenous amiodarone products.

### Key message for healthcare professionals:<sup>1</sup>

- Rare cases of cardiac arrest, life-threatening arrhythmias and hypotension have been reported in neonates and infants who have received amiodarone post-natally.

#### Reference

1. *Amiodarone syringe, Amiodarone hydrochloride for injection (amiodarone hydrochloride)* [product monograph]. Boucherville (QC): Sandoz Canada Inc.; 2016.

### Primaquine (primaquine phosphate)

The risk of **genotoxicity and embryo-fetal developmental toxicity** with primaquine use by the mother or father has been included in the *Warnings* section of the Canadian product monograph.

### Key messages for healthcare professionals:<sup>2</sup>

- The use of primaquine is contraindicated during pregnancy (even if a pregnant woman is glucose-6-phosphate dehydrogenase normal, the fetus may not be).
- Preclinical data show a potential risk of genotoxicity and a potential embryo-fetal developmental toxicity.
- Patients must be informed of the potential genotoxic risk.
- Patients have to avoid pregnancy during treatment and for the following period after end of treatment:
  - in treated women of childbearing potential, until completion of on-going ovulatory cycle (i.e., up to next menses),
  - in treated males whose partners may become pregnant, for 3 months.

#### Reference

2. *Primaquine (primaquine phosphate)* [product monograph]. Laval (QC): sanofi-aventis Canada Inc.; 2017.

### **Seroquel (quetiapine fumarate) and Seroquel XR (quetiapine fumarate extended-release)**

The risk of **misuse, abuse, tolerance, and/or physical dependence** has been included in the *Warnings and Precautions* section of the Canadian product monographs for Seroquel and Seroquel XR.

### **Key messages for healthcare professionals:<sup>3,4</sup>**

- There have been reports of quetiapine misuse, abuse, tolerance, and/or physical dependence.
- These cases include adult and adolescent patients using quetiapine alone or with other substances of abuse.
- Caution is needed when prescribing quetiapine to patients with a history of alcohol or drug abuse.
- Patients should be observed closely for signs of Seroquel / Seroquel XR misuse or abuse (e.g., development of tolerance, increases in dose, drug-seeking behavior), particularly if they have a history of alcohol or drug abuse.

#### References

3. *Seroquel (quetiapine fumarate immediate-release tablets)* [product monograph]. Mississauga (ON): AstraZeneca Canada Inc.; 2017.
4. *Seroquel XR (quetiapine fumarate extended-release tablets)* [product monograph]. Mississauga (ON): AstraZeneca Canada Inc.; 2017.

### **Tecfidera (dimethyl fumarate)**

The risk of **liver injury** has been included in the *Warnings and Precautions* and *Adverse Reactions* sections of the Canadian product monograph for Tecfidera (dimethyl fumarate).

### **Key messages for healthcare professionals:<sup>5</sup>**

- Clinically significant cases of liver injury have been reported in patients treated with Tecfidera in the postmarketing setting.
- Signs and symptoms of liver injury, including elevation of serum aminotransferases to greater than 5-fold the upper limit of normal and elevation of total bilirubin to greater than 2-fold the upper limit of normal have been observed.
- These abnormalities resolved upon treatment discontinuation.
- Some cases required hospitalization but none of the reported cases resulted in liver failure, liver transplant, or death.
- Discontinue Tecfidera if clinically significant liver injury induced by Tecfidera is suspected.

#### Reference

5. *Tecfidera (dimethyl fumarate)* [product monograph]. Mississauga (ON): Biogen Canada Inc.; 2017.

## Valproate products (valproic acid, divalproex sodium)

Additional information regarding the risk of **teratogenicity** has been added to the *Warnings and Precautions* section (including the boxed Serious Warnings and Precautions) of the Canadian product monographs (CPMs) for Depakene (valproic acid) and Epival (divalproex sodium).

Product labelling for both Depakene and Epival already contained information on the risk of birth defects (e.g., spina bifida), as well as the risk of developmental delay, autism and/or autism spectrum disorders and decreased IQ scores for children exposed *in utero*. Health Canada has also previously [communicated](#) on the risks to children who were exposed to valproate products *in utero*.

The CPMs were updated to provide further information and raise awareness of the risk of teratogenicity when using these products during pregnancy.

## Key messages for healthcare professionals:<sup>6,7</sup>

- Valproate products (valproic acid, divalproex sodium) **should not** be used in female children, in female adolescents, in women of childbearing potential and pregnant women unless alternative treatments are ineffective or not tolerated because of its high teratogenic potential and risk of developmental disorders in infants exposed *in utero* to valproate.
- Women of childbearing potential **must** use effective contraception during treatment and be informed of the risks associated with the use of valproate products during pregnancy.
- In women planning to become pregnant every effort should be made to switch to appropriate alternative treatment prior to conception.

### References

6. *Depakene (valproic acid)* [product monograph]. Etobicoke (ON): BGP Pharma ULC; 2017.
7. *Epival (divalproex sodium)* [product monograph]. Etobicoke (ON): BGP Pharma ULC; 2017.

### Did you know?

Health Canada is working with the manufacturer to update the Depakene and Epival packaging labels in order to reflect the warning for females of childbearing age, with the inclusion of a pictogram.



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## 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](#)
- [Drug Shortages Canada](#)

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## Suggestions?

Your comments are important to us. Let us know what you think by reaching us at [InfoWatch\\_InfoVigilance@hc-sc.gc.ca](mailto: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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