Important Safety Information on ALERTEC (modafinil) and the Risk of Congenital Anomalies

teva | Canada Innovation

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Audience
Healthcare professionals including psychiatrists, neurologists, respirologists, obstetricians, pediatricians, family physicians, general practitioners, nurses, and pharmacists.

Key messages

- **When used during pregnancy, ALERTEC (modafinil) has been associated with cases of major fetal congenital malformations, including congenital cardiac anomalies.**
- **ALERTEC is now contraindicated in women who are pregnant or may become pregnant. This information has been included in the *Contraindications, Warnings and Precautions,* and *Patient Medication Information* sections of the Canadian Product Monograph (CPM) for ALERTEC.**
- **Healthcare professionals are advised to discuss the following with all female patients of reproductive potential treated with, or to be treated with, ALERTEC:**
  - **the potential risks associated with ALERTEC to a fetus during pregnancy;**
  - **the need for a negative pregnancy test within a week before starting treatment with ALERTEC;**
  - **the necessity to use effective contraception during therapy with ALERTEC, and for two months after stopping ALERTEC treatment; and**
  - **the possible reduced effectiveness of steroidal contraceptives when using ALERTEC. Patients using steroidal contraceptives should use alternative or additional methods of contraception during the ALERTEC treatment, and for two months after stopping ALERTEC treatment.**
- **Health Canada, in collaboration with Teva Canada Innovation, updated the CPM for ALERTEC to reflect this new safety information. Health Canada will work with the manufacturers of generic versions of modafinil to update their respective CPMs.**

What is the issue?

In February 2019, TEVA Canada Innovation informed Health Canada of the results of the 2018 annual report of the ongoing Nuvigil/Provigil (modafinil) Pregnancy Registry in the United States. The results suggested a higher rate of major congenital anomalies, and other adverse reactions, in children exposed to the drug in utero.

Products affected

ALERTEC (modafinil) 100 mg tablets (DIN 02239665)

Other products affected by this risk information include all generic modafinil 100 mg tablets.

Background information

ALERTEC (modafinil 100 mg tablets) is indicated in Canada for the symptomatic treatment of excessive sleepiness in adult patients with narcolepsy, obstructive sleep apnea (OSA) and shift work disorder (SWD - a circadian rhythm sleep disorder).

After developmental toxicity was observed in animal studies, the Food and Drug Administration in the United States requested the initiation of the Nuvigil/Provigil Pregnancy Registry to characterize the pregnancy and fetal outcomes associated with Provigil (modafinil) and Nuvigil (armodafinil, the R-enantiomer of modafinil; not marketed in Canada) exposure during pregnancy.

In February 2019, TEVA Canada Innovation informed Health Canada of the results of the 2018 annual report of the Nuvigil/Provigil Pregnancy Registry. This report documented cases of spontaneous abortion and of major congenital anomalies, including cardiac congenital anomalies. The frequency of major congenital anomalies (17.3%) and cardiac anomalies (4%) associated with the exposure to modafinil and/or armodafinil was above the frequency observed in the general population (3% and 1%, respectively). There have also been post-marketing reports of congenital malformations and of low fetal growth, as well as cases of babies who failed to thrive (poor physical development).

Based on the findings from the Pregnancy Registry and from post-marketing cases reporting major congenital anomalies (e.g., cardiac anomalies, microcephaly), the CPM was updated to include a contraindication to the use of ALERTEC in pregnancy and to provide additional information on the findings of the registry.

Information for consumers

ALERTEC is used to treat adults who have excessive sleepiness due to one of the following medical conditions:

- Narcolepsy: People who have this condition experience sudden attacks of sleep that cannot be controlled.
- Obstructive Sleep Apnea (OSA): People with this condition have breathing problems during sleep.

- Shift Work Disorder (SWD): People with this condition experience very strong feelings of sleepiness when they work in shifts or irregular schedules outside the normal sleep period.

Findings from international post-marketing reports have showed that ALERTEC may cause harm to an unborn baby.

- Women who are pregnant, or plan to become pregnant, must not use ALERTEC.

- Hormonal birth control methods, such as birth control pills, injections, implants, intrauterine devices or patches, may not work as well when used at the same time as ALERTEC. Women who use these types of birth control may have a higher chance of getting pregnant while taking ALERTEC, and for two months after stopping ALERTEC. Patients should talk to a healthcare professional about birth control methods that are right for them while using ALERTEC.

- Women should take a pregnancy test within a week before starting treatment with ALERTEC and ensure they are not pregnant.

- Patients should discuss any questions or concerns about this information with their healthcare professional.

- Patients taking ALERTEC should also inform their healthcare professional if they experience any adverse reactions.

Information for healthcare professionals

- ALERTEC is contraindicated in women who are pregnant, or who may become pregnant.
- Healthcare professionals are advised to:
    - discuss with all female patients treated or to be treated with ALERTEC the potential risks associated with ALERTEC to a fetus during pregnancy;
    - ensure all female patients of reproductive potential have a negative pregnancy test within a week before starting treatment with ALERTEC;
    - instruct all female patients of reproductive potential that they must use effective contraception during therapy with ALERTEC, and for two months after discontinuation of ALERTEC treatment; and
    - inform female patients that ALERTEC may reduce the effectiveness of steroidal contraceptives and that alternative or concomitant methods of contraception, other than steroidal, are required during the ALERTEC treatment, and for two months after discontinuation of ALERTEC.

Action taken by Health Canada

Health Canada, in collaboration with Teva Canada Innovation, updated the CPM for ALERTEC. Health Canada will work with the manufacturers of generic versions of modafinil to update their respective CPMs. Health Canada is communicating this

important safety information to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site (https://healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php). This communication update will be further distributed through the MedEffect™ e-Notice email notification system, as well as through social media channels, including LinkedIn and Twitter.

Report health or safety concerns

Health Canada's ability to monitor the safety of marketed health products depends on healthcare providers and consumers reporting adverse reactions and medical device incidents. Any case of congenital anomalies, or other serious or unexpected adverse reactions, in patients receiving ALERTEC should be reported to Teva Canada Innovation or Health Canada.

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To correct your mailing address or fax number, contact Teva Canada Innovation.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate
E-mail: hc.mhpd-dpsc.sc@canada.ca
Telephone: 613-954-6522
Fax: 613-952-7738

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