Important Safety Information on TIVICAY, TRIUMEQ and JULUCA (dolutegravir containing medicines) – Possible Risk of Neural Tube Defects

2018/06/07

Audience
Healthcare professionals including infectious diseases specialists, Human Immunodeficiency Virus (HIV) specialists and nurses, clinical virologists, obstetricians, gynecologists, pediatricians, sexual health specialists, pharmacists and general practitioners

Key messages:

- **Early findings from the ongoing Tsepamo study in Botswana suggest a possible increased risk of neural tube defects (NTD) involving the brain, spine and spinal cord in infants born to women being treated with dolutegravir at the time of conception. No cases were reported in infants born to women who started dolutegravir during pregnancy.**

- **Although experience with the use of dolutegravir in pregnancy is limited, data from animal studies, as well as from the Antiretroviral Pregnancy Registry, clinical trials and post-marketing use, has not indicated a similar safety issue.**

- **Health professionals are advised to:**
  - **Avoid prescribing dolutegravir in women of childbearing potential (WOCBP) who are trying to become pregnant unless a suitable alternative treatment option is not available.**
  - **Consider the risk and benefits of dolutegravir treatment when prescribing it to WOCBP.**
  - **Inform WOCBP of the potential risk for NTD when dolutegravir is used at the time of conception and, as a precautionary measure, during the first trimester of pregnancy.**
  - **Perform pregnancy testing in WOCBP before initiating treatment.**
  - **Advise WOCBP who are taking dolutegravir to avoid getting pregnant and to use effective contraception throughout the treatment.**
  - **Switch to an alternative treatment when a pregnancy is confirmed in the first trimester while a woman is taking dolutegravir.**

- **The manufacturer will continue to monitor the results of the ongoing study and take appropriate action in consultation with Health Canada.**

What is the issue?
Serious cases of neural tube defects (NTD) in infants born to women with exposure to dolutegravir at the time of conception were identified in the ongoing observational study in Botswana. In the same study, no infant born to a woman who started dolutegravir during pregnancy had neural tube defects.

Products affected
TIVICAY (dolutegravir)
TRIUMEQ (dolutegravir, abacavir, lamivudine)
JULUCA (dolutegravir, rilpivirine)

Background information
TIVICAY in combination with other antiretroviral agents is indicated for the treatment of Human Immunodeficiency Virus (HIV-1) infection in adults and in Integrase Strand Transfer Inhibitor-naïve children at least 6 years of age and weighing at least 15 kg. TRIUMEQ is indicated for the treatment of HIV-1 infection in adults and adolescents aged 12 years and older and weighing at least 40 kg. JULUCA is used as a complete regimen to replace the current antiretroviral regimen for the treatment of HIV-1 infection in adults who are virologically stable and suppressed.

The preliminary analysis of the ongoing Tsepamo observational study in Botswana reported 4 cases of NTD out of 426 pregnancies in women who became pregnant while taking dolutegravir. This represents an incidence of about 0.9% compared to about 0.1% in patients receiving other non-dolutegravir treatments. No infant born to a woman who started dolutegravir during pregnancy had a NTD (N=0/2824).

The Tsepamo study is an ongoing birth outcomes surveillance study and further data will be captured during the ongoing surveillance over the next 9 months (May 2018 to February 2019). This data will provide more information about the safety of dolutegravir during pregnancy. It is anticipated that birth outcomes from at least another 600 women who have already become pregnant and who were on dolutegravir before conception will be captured in the ongoing surveillance.

Dolutegravir has been tested in a series of reproductive toxicology studies, including embryofetal development studies, and no relevant findings were identified.

Although there is limited experience with the use of dolutegravir in pregnancy, the data analysed to date from all sources including the Antiretroviral Pregnancy Registry (APR), clinical trials and post-marketing use has not indicated a similar potential safety issue. One additional case of NTD was reported spontaneously from Namibia.

There are no specific congenital abnormality signals (including NTD) from other sources when dolutegravir is started during pregnancy.

Information for consumers
Dolutegravir is a medication used to treat human immunodeficiency virus (HIV) infection.

Serious cases of neural tube defects have been reported in about 1% of babies born to women taking dolutegravir when they conceived and during their first trimester. Neural tube defects are birth defects of the brain, spine, and spinal cord.

Patients using dolutegravir should not stop taking it without first talking to their health care professional. Stopping their medicine can cause the HIV infection to worsen. Women planning to become pregnant and taking dolutegravir should discuss treatment options with their doctor before becoming pregnant. Women taking dolutegravir should avoid getting pregnant and use effective contraception.

Women who become pregnant while taking dolutegravir should consult with their doctor right away.

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

Information for health care professionals
Healthcare professionals are advised to:

- Avoid prescribing dolutegravir in women of child bearing potential (WOCBP), who are trying to become pregnant, unless a suitable alternative treatment option is not available.
- Consider the risk and benefits of prescribing dolutegravir in WOCBP.
- Perform pregnancy testing in WOCBP before initiating treatment.
- Advise women who are taking dolutegravir to avoid getting pregnant and use effective contraception throughout the treatment.
- Switch to an alternative treatment when a pregnancy is confirmed in the first trimester while a woman is taking dolutegravir.

Action taken by Health Canada
Health Canada is communicating this important safety information update to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site (www.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.

Report health or safety concerns
Managing marketed health product-related side effects depends on health care professionals and consumers reporting them. Any case of NTD or other serious or unexpected side effects in patients receiving TIVICAY, TRIUMEQ or JULUCA should be reported to ViiV Healthcare ULC or Health Canada.

ViiV Healthcare ULC
245, boulevard Armand-Frappier
Laval, Quebec
H7V 4A7
1-877-393-8448

To correct your mailing address or fax number, contact ViiV Healthcare ULC.

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: mhpd_dpsc@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

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