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IMPORTANT

MEDICINE SAFETY INFORMATION

ViiV Healthcare SAFETY TIVICAY / TRELAVUE

Date: 12 June 2018

Dear Healthcare Professional

Title: TIVICAY (reg. no.: 48/20.2.8/0403) dolutegravir, TRELAVUE (reg. no.: 49/20.2.8/0097) dolutegravir/abacavir/lamivudine: Risk of neural tube defects reported in Tsepamo Study, Botswana

Key Messages

ViiV Healthcare would like to inform you of a potential safety issue which has been brought to our attention by the Principal Investigator of the above study conducted in Botswana. The potential safety issue is related to Neural Tube Defect (NTD) cases in infants born to women with exposure to dolutegravir-containing regimens *at the time of conception* identified from a preliminary unscheduled analysis of the Tsepamo study (4 NTD cases out of 426 pregnancies on dolutegravir). This represents an incidence of about 0.9% with an expected background rate of about 0.1%.

In the same study, no infant born to a woman who started dolutegravir *during pregnancy* had a neural tube defect (N=0/2824).

While this safety signal is being evaluated, ViiV Healthcare recommends the following:

- In women of child bearing potential (WOCBP) pregnancy testing should be performed before initiation of Tivicay/Trelavue treatment.
- WOCBP who are taking Tivicay/Trelavue should avoid getting pregnant and should use effective contraception throughout treatment.
- In WOCBP who are actively seeking to become pregnant, it is recommended to avoid Tivicay/Trelavue based regimens.
- If a woman becomes pregnant while taking Tivicay/Trelavue and the pregnancy is confirmed in the first trimester, it is recommended to switch to a safe alternative regimen.

Supporting information

- The Tsepamo study is a birth outcomes surveillance study which is ongoing and further data will be captured during the ongoing surveillance. This information will help to further inform 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 were on dolutegravir from prior to conception will be captured in the ongoing surveillance over the next 9 months (May 2018 to February 2019).
- Dolutegravir was tested in a complete package of reproductive toxicology studies, including embryofoetal development studies, and no relevant findings were identified.
- There are no specific congenital abnormality signals (including NTD) from other sources when dolutegravir is started during pregnancy.

Action Being Taken by ViiV Healthcare

- ViiV Healthcare will continue evaluating the full body of data for dolutegravir in pregnancy, and explore further options for data generation. This includes evaluating several different databases to determine if other cases have been observed.
- ViiV Healthcare will also continue collaborating with the study investigators and key stakeholders including Regulatory Agencies.
- The product information of Tivicay/Trelavue will be updated accordingly and further information will be communicated as appropriate.

Current Package Insert

The current labelling for dolutegravir-containing products states:

Tivicay:
Safe use during pregnancy and lactation has not been established. The effect of Tivicay on human pregnancy is unknown.

Trelavue:
The safe use of Trelavue in human pregnancy has not been established.

SAHPRA guidance: The foetus is most vulnerable to risk of major malformations, including NTDs, when exposed early in the pregnancy to a teratogenic medicine.

For questions, medical information requests or to report any suspected adverse drug reaction please contact GlaxoSmithKline South Africa (Pty) Limited (GSK) via email at: **mu.zinchub@gsk.com**

You can also assist in the monitoring of drug safety by reporting suspected adverse drug reactions to the National Drug Adverse Event Monitoring Centre (NADEMC) at Tel: 021 – 447 1618; Fax: 021 -448 6181

Yours sincerely

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