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Tivicay▼ (dolutegravir),Triumeq▼ (dolutegravir,abacavir,lamivudine), Juluca▼ (dolutegravir,rilpivirine): neural tube defects reported in infants born to women exposed to dolutegravir at the time of conception

Dear Healthcare Professional

ViiV Healthcare, in agreement with the European Medicines Agency, would like to inform you of the following:

Summary
In an ongoing birth outcome surveillance study, conducted in Botswana, the Tsepamo study, 4 cases of neural tube defects (NTD) have been reported in 426 infants born to women who took dolutegravir as part of combined antiretroviral therapy at the time of conception. This represents an incidence of about 0.9% compared with an expected background rate of about 0.1% in infants born to women taking other antiretroviral medicines at the time of conception.

While this safety signal is being evaluated, the following measures are recommended:

- **In women of child bearing potential (WOCBP) pregnancy testing should be performed and pregnancy should be excluded before initiation of treatment.**
- **WOCBP who are taking dolutegravir should use effective contraception throughout treatment.**
- **In WOCBP who are actively seeking to become pregnant, it is recommended to avoid dolutegravir.**
- **In case a woman becomes pregnant while taking dolutegravir and the pregnancy is confirmed in the first trimester, it is recommended to switch to an alternative treatment unless there is no suitable alternative.**

Background information
The issue has been identified from a preliminary unscheduled analysis of the ongoing Tsepamo study in Botswana. Further data from this study will be captured during the ongoing surveillance. This information will help to further inform about the safety of dolutegravir during pregnancy.

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Although there is limited experience with the use of dolutegravir in pregnancy, the currently available data from other sources including Antiretroviral Pregnancy Registry, clinical trials and post-marketing use has not indicated a similar safety issue. There is only one other report of NTD reported spontaneously from Namibia in which dolutegravir was used a few months prior to conception and during pregnancy.

There are currently no congenital abnormality signals (including NTD) associated with the use of dolutegravir during pregnancy from other data sources. Dolutegravir was tested in a complete package of reproductive toxicology studies, including embryofetal development studies, and no relevant findings were identified.

Neural tube defects occur when the neural tube fails to completely form (between 0 and 28 days after conception), and the spinal cord, brain and related structures do not form properly.

This new finding is being considered in the context of other available data and the product information of TIVICAY/TRIUMEQ/JULUCA will be updated accordingly and further information will be communicated as appropriate.

Call for reporting
Adverse events should be reported. For the UK, reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellowcard in the Google Play or Apple App store. Adverse events should also be reported to GSK UK Safety Team on 0800 221 441 selecting option 3 or email UK PharmaSafety team (uksafety@gsk.com).

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Company contact point
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