REPUBLIC OF NAMIBIA

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OFFICE OF THE REGISTRAR OF MEDICINES

DEAR HEALTHCARE PROFESSIONAL

COMMUNICATION OF RECOMMENDATIONS ON DOLUTEGRAVIR IN RESPONSE TO THE POTENTIAL RISK OF BIRTH DEFECTS IN PREGNANCY

Background

This communication follows an identified potential safety issue with the HIV antiretroviral medicine dolutegravir (Tivicay®). The safety issue was identified from the findings of an on-going observational study in Botswana, which found 4 (four) cases of neural tube defects, out of 426 women who became pregnant while taking dolutegravir in combination with other antiretrovirals. This rate of 0, 9 % is higher than the rate of approximately 0, 1 % seen in women who were taking other non-dolutegravir antiretroviral combination medicines in this setting. The findings have been found to be statistically significant.

There were no reported cases of neural tube defects in women started on dolutegravir later in pregnancy. Additional data is expected from the Botswana study and other settings where women have already been exposed to dolutegravir at the time of conception or early in the first trimester but who has not yet delivered.

Based on these preliminary findings, women who fall pregnant while on dolutegravir or who are initiated on dolutegravir early in the first trimester may be at increased risk of giving birth to babies with these specific birth defects.

Dolutegravir is registered with the Namibia Medicines Regulatory Council under the brand name Tivicay® and is therefore available. Although dolutegravir is not yet included in the current National Guidelines for Antiretroviral Therapy as a first line agent, it is reserved for

third line. It has however also been noted that some patients who are "In-Transit" from countries which have included it in the first line receiving are receiving dolutegravir.

Namibia Medicines Regulatory Council (NMRC)'s recommendations

In light of this new concern about the safety of dolutegravir use in pregnancy, NMRC is issuing the following precautionary recommendations:

- Healthcare professionals should follow the current ART guidelines (National Guidelines for Antiretroviral Therapy Fifth Edition) and any additional guidance from the Directorate of Special Programs (DSP).
- ARV therapy for women and adolescents of childbearing age, including those who are pregnant, should be based on medicines for which adequate efficacy and safety data are available; an efavirenz-based regimen is a safe and effective first-line regimen.
- Women who are trying to fall pregnant should not be prescribed dolutegravir.
- If other first-line ARVs cannot be used in women and adolescents of childbearing age, for example due to drug resistance to efavirenz, dolutegravir may be considered in cases where consistent contraception can be assured.
- Healthcare professionals should weigh the benefits and the risks of dolutegravir when prescribing antiretroviral medicines to women of childbearing age. Alternative antiretroviral medicines should be considered. Discuss the relative risks and benefits of appropriate alternative antiretroviral therapies.
- If the decision is made to use dolutegravir in women of childbearing age, health care professionals should reinforce the consistent use of effective birth control.
- Healthcare professionals should inform women of childbearing age about the potential risk of neural tube defects when a dolutegravir-containing regimen is used at the time of conception and early in pregnancy.
- Pregnancy testing should be performed before initiation of a dolutegravir-containing regimen in women of childbearing age to exclude pregnancy.

Call to report adverse medicine reactions

Data on the safety of medicines in pregnancy is often lacking or inadequate at the time of marketing approval of a medicine, and post-marketing surveillance is essential to ensure that these medicines are safe, including in pregnancy, and are effective and of good quality.

Healthcare professionals in Namibia are therefore urged to report all adverse events or side effects related to the use of dolutegravir by completing the Adverse Medicines Reaction Form (Safety Yellow Form) to the Therapeutics Information & Pharmacovigilance Centre (TIPC) of the NMRC.

Please see below the contact details for TIPC:

Tel: 061 203 2406
Fax: 086 451 8283
Email: info.TIPC@mhss.gov.na

NMRC will continue to collect more data on the safety of dolutegravir in pregnancy as it becomes available and will review its recommendations and update the healthcare professionals accordingly.

Yours Sincerely,

MR. JOHANNES GAESEB
REGISTRAR OF MEDICINES