

TECHNICAL BRIEF

Dolutegravir for women living with HIV of reproductive age

A recently reported safety issue with dolutegravir, an antiretroviral drug used to treat and prevent HIV infection, is leading to concerns around reproductive and treatment coercion for women and adolescent girls of reproductive age.

Purpose

In May 2018, the World Health Organization (WHO) reported a potential safety issue concerning dolutegravir (DTG), a common first-line antiretroviral treatment drug that is used to prevent and treat HIV infections. Preliminary findings from a study in Botswana found an increased risk of neural tube defects in infants born to women taking DTG at the time of conception. As a result of this study, WHO's revised guidance on antiretroviral regimens for treating and preventing HIV infections, released in July 2018, include a caution on use of DTG by women and adolescent girls of childbearing potential. This brief aims to provide an overview of the research to date, current WHO guidance, and recommendations for IPPF.

Background

In 2016, WHO released consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infections. These guidelines recommended efavirenz (EFV)-based regimens as the preferred first-line ART for people living with HIV. Due to limited published data on the safety of DTG during pregnancy and breastfeeding, it was recommended as an alternative to EFV.

Since publication, several studies have explored the safety and efficacy of DTG during pregnancy. A 2018 systematic review found that DTG-based regimens were more effective than EFV at suppressing viral load and increasing CD4 cell count. DTG also has a lower potential for drug interactions, can be cheaper to produce, has a lower potential for drug resistance, and is active against HIV-2 infection.

In May 2018, WHO reported a safety concern that affects women living with HIV using DTG at the time of conception. An ongoing observational study in Botswana found four cases of neural tube defects (birth defects of the brain, spine or spinal cord) out of 426 women who became pregnant while they were using DTG. This is a rate of about 0.9%,

compared to 0.1% among women who were taking non-DTG-based ART regimens.

With new evidence, WHO issued interim guidance in July 2018, stating that DTG-based regimens are the preferred first-line ART for all people living with HIV over six years old, including adolescent girls and women of childbearing potential who are using consistent and reliable contraception. The guidance acknowledges the preliminary nature of the data and states that guidance will be updated as soon as more information is available.

WHO Recommendation

The interim guidance states that **a DTG-based regimen may be recommended as a preferred first-line regimen for people living with HIV initiating ART**. This includes use by adults and adolescents (moderate-certainty evidence); women and adolescent girls of childbearing potential (very-low-certainty evidence); and infants and children with approved DTG dosing (low-certainty evidence).

However, the guidance also includes a **note of caution on using DTG during the periconception period and for women and adolescent girls of childbearing potential**. The guidance highlights that:

- Exposure to DTG at the time of conception may be associated with neural tube defects among infants.
- DTG appears to be safe when started later in pregnancy: after the period of risk of neural tube defects, up to eight weeks after conception.
- Adolescent girls and women of childbearing potential who do not currently want to become pregnant can receive DTG together with consistent and reliable contraception. There are no reported interactions between DTG and hormonal contraception, although the data is limited.
- An EFV-based regimen is a safe and effective first-line regimen and can be used among women of childbearing potential during the period of potential risk for developing neural tube defects.

IPPF Member Associations should guide and counsel women through their HIV treatment and contraception options to ensure they can fully exercise their sexual and reproductive health and rights.

This Technical Brief was prepared by the IPPF Technical Team. Please contact Hayley Gleeson, Technical Adviser HIV, with any questions (hgleeson@ippf.org)

Implications for IPPF

IPPF is concerned that these preliminary findings, and potential responses from countries and health care providers, could limit women's full freedom to control their own health and bodies.

Organizations led by women living with HIV have raised concerns that the WHO recommendation undermines women's choice by prioritizing reproductive success over treatment success: that is, women of reproductive age who do not (or cannot) use modern contraceptive methods may be denied access to DTG or may be switched to alternative (potentially less effective) treatment regimens without their fully informed consent. Where women and adolescent girls want to continue using DTG, there are concerns that they may be coerced into using contraception, sterilization or abortion without their consent.

Countries may also decide not to adopt DTG as a first-line regimen due to these findings, therefore denying people living with HIV the right to access more effective HIV treatment. This is particularly important in areas where access to reliable and consistent contraception cannot be guaranteed and where there remains a high unmet need for family planning.

ADVOCATES

This is an important opportunity for IPPF to continue advocating for access to comprehensive family planning services, including long-acting reversible methods of contraception (LARCs) and to safe abortion care. All women have the right to decide about their own health care, and this includes the choice about their ARVs and their contraception. Women should have access to full information about their HIV treatment and contraception options, including potential risks and benefits. Women living with HIV must have access not only to the most effective HIV treatment, but also to a range of modern contraceptive methods, in order to fully take control over their sexual and reproductive lives.

Advocacy messaging should emphasize a woman's right to choose whether and when to have children, and should seek to ensure a secure supply of sexual and reproductive health commodities and supplies including treatment for HIV and other sexually transmitted infections, contraceptives, emergency contraceptives, male and female condoms and misoprostol for safe abortion and post-abortion care. Advocates and Member Associations should also work with governments and ministries of health to ensure access to DTG and a range of contraceptive methods, including LARCs.

SERVICE PROVIDERS

Clients may be very worried about this evidence and the WHO guidance could impact them and their health. Service providers should:

- Uphold a rights-based approach as they counsel and guide women through treatment decisions, ensuring that all health care is people-centred and that all decisions about treatment and care are made together.
- Support women who choose to use DTG-based regimens and counsel them on the possible increased risk during the periconception period. If a woman becomes pregnant while using DTG, they should be supported through all their treatment and reproductive decisions.
- Support women who choose to transition to an EFV-based regimen and respect their right to decide on the timing of their pregnancies.
- Support women to adhere to their ART regimen and provide information on the full range of contraceptive methods available to them, including access to male and female condoms.
- Counsel women on emergency contraception and safe abortion care.
- Remain aware of any updated research or guidance on this topic and ensure rapid dissemination throughout their networks.

Useful resources

WHO Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV

<http://www.who.int/hiv/pub/guidelines/ARV2018update/en/>

WHO Statement on the potential safety issue affecting women living with HIV using dolutegravir at the time of conception

http://www.who.int/medicines/publications/drugalerts/Statement_on_DTG_18May_2018final.pdf

IPPF Press Release on Dolutegravir and Reproductive Coercion

<https://www.ippf.org/news/no-coercion-treatment-options-women-living-hiv>

IPPF IMAP Statement on Zika virus and sexual and reproductive health

https://www.ippf.org/sites/default/files/ippf_imap_zika_web.pdf