

Direct Healthcare Professional Communication

26th March 2019
HIV/UK/19-03/CI/1223

Genvoya[®]▼ (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide)
Stribild[®] (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil)
Tybost[®] (cobicistat)

Increased risk of treatment failure and increased risk of mother-to-child transmission of HIV infection due to lower exposure of elvitegravir and cobicistat during the second and third trimesters of pregnancy

Dear Healthcare professional,

Gilead Sciences, in agreement with the European Medicines Agency and the UK Medicines and Healthcare Products Regulatory Agency (MHRA), would like to inform you of the following:

Summary

- **Therapy with elvitegravir/cobicistat should not be initiated during pregnancy.**
- **Women who become pregnant during therapy with elvitegravir/cobicistat should be switched to an alternative regimen.**
- **This is because pharmacokinetic data showed lower exposures of cobicistat and elvitegravir during the second and third trimesters of pregnancy.**
- **Lower elvitegravir exposure may be associated with an increased risk of treatment failure and an increased risk of mother-to-child transmission of HIV infection.**

Background

In June 2018, a Direct Healthcare Professional Communication was distributed relating to the increased risk of treatment failure and mother-to-child transmission of HIV infection due to lower exposures of darunavir boosted with cobicistat during pregnancy.

The risk of this occurring in treatments containing elvitegravir/cobicistat has also been reviewed. Pharmacokinetic data from the IMPAACT P1026s (International Maternal Pediatric Adolescent AIDS Clinical Trials) study has shown that compared with paired postpartum data, plasma concentration after 24 hours of elvitegravir boosted with cobicistat was 81% lower in the second trimester and 89% lower in the third trimester. Plasma concentration after 24 hours of cobicistat was 60% and

76% lower in the second and third trimester, respectively. The proportion of pregnant women who were virologically suppressed was 76.5% in the second trimester, 92.3% in the third trimester, and 76% postpartum. A review of data from this prospective study, pregnancy cases from other clinical trials, the Gilead global safety database, and published literature, has not identified any cases of mother-to-child HIV-1 transmission in women taking regimens containing elvitegravir/cobicistat during the second and third trimesters of pregnancy.

The reduction in elvitegravir exposure may result in virological failure and an increased risk of mother-to-child transmission of HIV infection. Therefore, therapy with elvitegravir/cobicistat should not be initiated during pregnancy, and women who become pregnant during therapy with elvitegravir/cobicistat should be switched to an alternative regimen.

The product information for Genvoya and Stribild will be updated with this recommendation. The product information for Tybost will be updated to reflect that darunavir/ cobicistat should not be initiated during pregnancy to align with advice previously issued with darunavir boosted with cobicistat during pregnancy.

Call for reporting

Healthcare professionals are reminded to continue to report suspected adverse reactions associated with Genvoya▼, Stribild, and Tybost in accordance with the national spontaneous reporting system.

Please continue to report suspected adverse reactions to the MHRA through the Yellow Card Scheme. Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle▼

It is easiest and quickest to report ADRs online via the Yellow Card website: <https://yellowcard.mhra.gov.uk>, or via the Yellow Card app available from the Apple App Store or Google Play Store.

Alternatively, prepaid Yellow Cards for reporting are available:

- upon request by mail: "FREEPOST YELLOW CARD" (no other address details necessary)
- by emailing yellowcard@mhra.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- by electronic download through the Yellow Card section of the MHRA website

When reporting a suspected adverse reaction, please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates.

Suspected adverse reactions may also be reported to Gilead via email to Safety_FC@gilead.com or by telephone +44 (0) 1223 897500.

Company contact point

Contact Gilead Sciences Medical Information at Telephone: +44 (0) 8000 113700 or E-mail: ukmedinfo@gilead.com if you have additional questions.

Annexes

More information about the IMPAACT P1026s study can be found here: <https://www.ncbi.nlm.nih.gov/pubmed/30134297>

Yours Sincerely,



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Gilead Sciences Ltd