Direct Healthcare Professional Communication

06 June 2018

Darunavir/cobicistat: Increased risk of treatment failure and increased risk of mother-to-child transmission of HIV infection due to low exposure values of darunavir and cobicistat during the second and third trimesters of pregnancy

Dear Healthcare Professional,

Janssen-Cilag International N.V. in agreement with the European Medicines Agency (EMA) and the Medicines Authority (MA) would like to inform you of the following:

Summary

- **Therapy with darunavir/cobicistat should not be initiated during pregnancy.**
- **Women who become pregnant during therapy with darunavir/cobicistat should be switched to an alternative regimen: darunavir/ritonavir may be considered as an alternative.**
- **This is because pharmacokinetic data showed low exposure values of darunavir and cobicistat during the second and third trimesters of pregnancy.**
- **Low darunavir exposure may be associated with an increased risk of treatment failure and an increased risk of mother-to-child transmission of HIV infection.**

Background

The pharmacokinetic data from the Phase 3b study TMC114HIV3015 in 6 pregnant women demonstrated that the mean exposure (AUC) of darunavir boosted with cobicistat was 56% and 50% lower during the 2nd and 3rd trimesters of pregnancy, respectively, compared with 6 to 12 weeks postpartum. Mean darunavir C_{min} concentrations were around 90% lower during the 2nd and 3rd trimesters of pregnancy as compared to postpartum. Exposure of cobicistat was 63% and 49% lower during the 2nd and 3rd trimesters of pregnancy, respectively, as compared to postpartum.

Low darunavir exposure may be associated with an increased risk of treatment failure and an increased risk of HIV-1 transmission to the child. Therefore, therapy with darunavir/cobicistat should not be initiated during pregnancy and women who become pregnant during therapy with darunavir/cobicistat should be switched to an alternative regimen.

Based upon this information, the product information for PREZISTA, ▼REZOLSTA and ▼SYMTUZA will be updated, as recommended by the European Medicines Agency (EMA).

Contact information

▼ Rezolsta and Symtuza are subject to additional monitoring

Healthcare professionals are encouraged to report adverse events in patients taking PREZISTA, REZOLSTA and SYMTUZA in accordance with the national spontaneous reporting system.

Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form available online at http://www.medicinesauthority.gov.mt/adrportal and sent to Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN or sent by email to: postlicensing.medicinesauthority@gov.mt.

If you have further questions or require additional information, please contact:

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Yours Sincerely,

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