

## Direct Healthcare Professional Communication

22 June 2018

**Prezista® (darunavir), Rezolsta®▼ (darunavir/cobicistat) and Symtuza®▼ (darunavir/cobicistat/emtricitabine/tenofovir alafenamide)**

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

Dear Healthcare Professional,

Janssen in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) 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 (darunavir), REZOLSTA (darunavir and cobicistat) and SYMTUZA (darunavir, cobicistat, emtricitabine, tenofovir alafenamide), will be updated, as recommended by the European Medicines Agency (EMA).

### **Call for reporting**

**▼ This medicinal product is subject to additional monitoring to support risk management and it is therefore important to report any suspected adverse events.**

Please continue to report suspected adverse reactions with any medicine or vaccine to the MHRA through the Yellow Card Scheme.

It is easiest and quickest to report adverse drug reactions online via the Yellow Card website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

Alternatively, prepaid Yellow Cards for reporting are available by writing to FREEPOST YELLOW CARD (no other address details necessary), by emailing [yellowcard@mhra.gov.uk](mailto: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, or by downloading and printing a form from the Yellow Card section of the MHRA website.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, product brand name and batch numbers.

Suspected adverse reactions should also be reported to Janssen-Cilag Limited on telephone: 01494 567447, fax: 01494 567799 or by email at [dsafety@its.jnj.com](mailto:dsafety@its.jnj.com).

### **Company contact points**

If you have further questions or require additional information, please contact: Janssen-Cilag Ltd. Medical Information Department: email: [medinfo@its.jnj.com](mailto:medinfo@its.jnj.com), telephone: 0800 731 8450 or 01494 567 444.

Yours faithfully,

  
**Dr Frank Wiegand**  
Medical Director  
Janssen UK & Ireland