

Ref: RA-08-200 / DAR 00 04

10 June 2008

Dear Healthcare Professional

### **PREZISTA<sup>®</sup> darunavir – New Product Information concerning hepatotoxicity**

Tibotec, a division of Janssen-Cilag Pty Ltd, would like to inform you of an important update to the Product Information for PREZISTA<sup>®</sup> darunavir tablets, regarding the addition of a precaution on hepatotoxicity.

In clinical trials and postmarketing experience, drug-induced hepatitis (e.g., acute hepatitis, cytolytic hepatitis) has been reported in patients receiving combination therapy with PREZISTA/rtv. Given the clinical relevance of this adverse reaction, the following information on hepatotoxicity has been added to the **Precautions** section of the PREZISTA **Product Information**:

#### **Hepatotoxicity**

*Drug-induced hepatitis (e.g., acute hepatitis, cytolytic hepatitis) has been reported with PREZISTA/rtv. During the clinical development program (N=3063), hepatitis has been reported in 0.5% of patients receiving combination therapy with PREZISTA/rtv. Patients with pre-existing liver dysfunction, including chronic active hepatitis B or C, have an increased risk for liver function abnormalities including severe hepatic adverse events.*

*Post-marketing cases of liver injury, including some fatalities, have been reported. These have generally occurred in patients with advanced HIV-1 disease taking multiple concomitant medications, having co-morbidities including hepatitis B or C co-infection, and/or developing immune reconstitution syndrome. A causal relationship with PREZISTA/rtv therapy has not been established.*

*Appropriate laboratory testing should be conducted prior to initiating therapy with PREZISTA/rtv and patients should be monitored during treatment. Increased AST/ALT monitoring should be considered in patients with underlying chronic hepatitis, cirrhosis, or in patients who have pre-treatment elevations of transaminases, especially during the first several months of PREZISTA/rtv treatment.*

*If there is evidence of new or worsening liver dysfunction (including clinically significant elevation of liver enzymes and/or symptoms such as fatigue, anorexia, nausea, jaundice, dark urine, liver tenderness, hepatomegaly) in patients on PREZISTA/rtv, interruption or discontinuation of treatment must be considered.*

In addition, the **Adverse Reactions** section of the PREZISTA Product Information has been updated to include this new information as well as information on the effects of combination antiretroviral therapy. The Australian **Consumer Medicine Information** has also been updated.

Please find attached to this communication the updated PREZISTA Product Information and Consumer Medicine Information (updated May 2008). Tibotec, a division of Janssen-Cilag is committed to ensuring that PREZISTA is used safely and effectively and providing you with the most current information for our products.

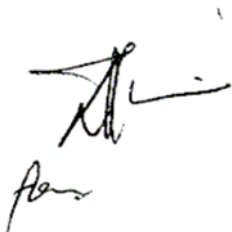
It is important that healthcare professionals and consumers report serious or unexpected adverse reactions to medicines. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with medicines. Any case of hepatotoxicity, or other serious or unexpected adverse reactions in patients receiving PREZISTA, should be reported to Janssen-Cilag Pty Ltd or the Therapeutic Goods Administration as follows:

Janssen-Cilag Pty Ltd Drug Safety  
Telephone: 1800 226 334 (Toll-free)  
e-mail: LSO\_AUST@janau.jnj.com  
Fax: (02) 9888 9817

Therapeutic Goods Administration: Adverse Drugs Reaction Unit  
Telephone: 1800 044 114 (freecall)  
e-mail: adrac@tga.gov.au  
Fax: (02) 6232 8392  
Website: [www.tga.gov.au/problem](http://www.tga.gov.au/problem)

For more information, please contact your Janssen-Cilag representative or telephone Janssen-Cilag Medical Information on 1800 226 334 (Toll free).

Yours faithfully,  
**Janssen-Cilag Pty Ltd**

A handwritten signature in black ink, appearing to read 'Malcolm Handel', with a horizontal line extending to the right.

Dr Malcolm Handel MB BS FRACP  
Medical Director