Costa Rica, June 3th, 2014

Subject: **Direct Healthcare Professional Communication**

IMPORTANT SAFETY UPDATE OF PRESCRIBING INFORMATION FOR COREG® (CARVEDILOL)

Dear Healthcare Provider,

F. Hoffmann-La Roche Ltd (hereafter referred to as Roche) would like to inform you about important new safety information for Coreg® (carvedilol) regarding severe cutaneous adverse reactions (SCAR), which has resulted in an update to the Warnings and Precautions and the Post-Marketing Undesirable Effects section of the product information/package insert for Coreg.

This letter is being sent after informing the National Competent Health Authority.

Summary

- Very rare cases of severe cutaneous adverse reactions such as toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) have been reported during treatment with carvedilol.
- Carvedilol should be permanently discontinued in patients who experience severe cutaneous adverse reactions possibly attributable to carvedilol.

Further Information

During 24 years of post-marketing surveillance (cumulative exposure over 32 million patients), very rare cases of severe cutaneous adverse reactions have been reported with carvedilol to the company safety database. The analysis of these cases identified one literature case with a fatal event of TEN probably causally related to treatment with carvedilol, and a second case reporting SJS possibly causally related to treatment with carvedilol.

As a consequence, the Warnings and Precautions and the Post-Marketing Undesirable Effects section of the Coreg product information/package insert has been updated with this important new safety information.

The following new information has been included in the product information/package insert for Coreg:

2.4 Warnings and Precautions

Severe cutaneous adverse reactions (SCARs)

Very rare cases of severe cutaneous adverse reactions such as toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) have been reported during treatment with carvedilol [see section 2.6.2 Postmarketing (Undesirable Effects)]. Carvedilol should be permanently discontinued in patients who experience severe cutaneous adverse reactions possibly attributable to carvedilol.

2.6.2 Post Marketing

Skin and subcutaneous tissue disorders

Severe cutaneous adverse reactions (Toxic epidermal necrolysis, Stevens-Johnson syndrome (see section 2.4 Warnings and Precautions)

If you have any questions or require additional information regarding the use of Coreg (carvedilol), please contact cac.medical_info@roche.com

Reporting Adverse Events

Roche will continue to monitor the safety of Coreg (carvedilol) through established reporting mechanisms and notify regulatory authorities of any serious adverse events for evaluation. We will continue to provide you with the most current Prescribing Information for Coreg (carvedilol) moving forward. You can assist us in monitoring the safety of Coreg (carvedilol) by reporting suspected adverse events associated with the use of Coreg (carvedilol) to cac.farmacovigilancia@roche.com or +506-2298-1500 / US toll free 1-888-670-4123..

Sincerely Yours,

Roche Servicios, S. A.

Should you have any questions or require additional information regarding the use of Coreg®, please contact: cac.medical_info@roche.com

To report an adverse event of Coreg® or any other Roche product, please contact: cac.farmacovigilancia@roche.com