Costa Rica, 18th February, 2016

IMPORTANT DRUG WARNING - ERIVEDGE®

Subject: Extension of Pregnancy Prevention Duration for Women of Childbearing Potential and Waiting Periods for Blood Donation and Lactation

Dear Healthcare Professional,

Roche would like to inform you of the following:

*Summary*

- The recommendation for Erivedge® contraceptive duration in women of childbearing potential has changed from 7 months to 9 months after the last dose.
- This new recommendation is based on an updated population pharmacokinetic modeling analysis.
- The waiting periods post-treatment for blood donation and lactation are also being modified from 7 to 9 months, based on the above findings.

There is no change in the current contraceptive advice for male patients, which is:
"Vismodegib is present in semen. To avoid potential embryo-fetal exposure during pregnancy, male patients must use condoms (with spermicide where available), even after a vasectomy, during sexual intercourse with women while being treated with Erivedge® and for 2 months after the last dose.
Male patients should not donate semen while being treated with Erivedge® and for 2 months after the final dose."

Additional information about this change is provided in the remainder of this letter.

*Prescriber Action*

Counsel patients about the teratogenic risk of Erivedge® and the need for contraception during and after treatment.

*Further information on the Changes to the Prescribing Information*

Teratogenicity is an important risk for patients using Erivedge®. At the time of Erivedge's® approval, there were limited population pharmacokinetic (popPK) data that supported the initial contraception recommendation. Recently, a post approval study of Erivedge® provided additional PK data up to 12

months after last dose. PK profiles were simulated and the pregnancy prevention duration was assessed by comparing the popPK simulated profile to the threshold of concern for teratogenic risk. The duration of time for the drug concentration to fall below the threshold for teratogenic risk is 7.4 months with a 90% confidence interval that ranges between 6-9 months.

The waiting period for lactation and blood donation is likewise being changed to 9 months based on this popPK estimate. There is no change in the current contraceptive advice for male patients based on popPK estimation. However, it is important to recognize that Erivedge® is present in semen, and male patients of all ages, who do not follow the pregnancy prevention plan, are at risk to expose women of childbearing potential to Erivedge®. Physicians are reminded to educate patients on the teratogenic risk of Erivedge® and the pregnancy prevention plan.

Roche is working to update the product information as soon as possible.

Erivedge® is indicated for the treatment of adult patients with advanced basal cell carcinoma for whom surgery is inappropriate.

*Call for reporting*

Health care professionals should report any serious adverse events suspected to be associated with the use of Erivedge® to: cac.farmacovigilancia@roche.com.

*Company contact point*

Should you have any questions regarding the use of Erivedge®, please feel free to contact us at: cac.medical_info@roche.com.

Sincerely,

ROCHE SERVICIOS S.A.