Subject: Erivedge ®▼ (vismodegib): important information to support safe use, including Pregnancy Prevention Programme

February 2014

Dear Healthcare Professional,

This letter is sent in agreement with the European Medicines Agency and Medicines Authority to inform you of important safety information regarding teratogenic effects and the introduction of a Pregnancy Prevention Programme for Erivedge, 150-mg hard capsules. Erivedge is indicated for the treatment of adult patients with symptomatic metastatic basal cell carcinoma or locally advanced basal cell carcinoma inappropriate for surgery or radiotherapy.

Summary

- **Erivedge has teratogenic effects. It may cause embryo-foetal death or severe birth defects and must not be used during pregnancy.**
- **A Pregnancy Prevention Programme (PPP) is in place for this medicine. Pregnancy prevention measures during and after treatment are required for women of childbearing potential and for men since Erivedge can be present in semen.**
- **Erivedge should only be prescribed by, or under the supervision, of a specialist healthcare professional experienced in the management of the approved indications.**
- **As a prescriber you must ensure:**
    - **that all patients are fully informed regarding the teratogenic effects of Erivedge**
    - **that patients are advised that Erivedge must not be given to another person, and that they must dispose of any unused capsules at the end of treatment in accordance with local requirements (e.g. returning unused capsules to the pharmacy)**
    - **that all patients, including men and women of non-childbearing potential, must receive the Patient Information Brochure and Reminder Card that summarise the measures of the PPP to be followed**
    - **that all patients are counselled and complete and sign a Verification of Counselling Form (VCF).**

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Further information on the safety concern

Hedgehog pathway inhibitors such as vismodegib have been demonstrated to be embryotoxic and/or teratogenic in multiple animal species and can cause severe malformations, including craniofacial anomalies, midline defects and limb defects. Erivedge may cause embryo-foetal death or severe birth defects when administered to a pregnant woman. Since Erivedge must not be used during pregnancy a PPP has been developed.

Before starting treatment with Erivedge

Women of childbearing potential (for definition, refer to the enclosed SmPC or Healthcare Professional Brochure)

Pregnancy testing
In these women, a pregnancy test conducted by a healthcare provider should be done within 7 days before initiating treatment. Pregnancy tests should have a minimum sensitivity of 25 mIU/mL human chorionic gonadotropin (hCG) or as per local availability.

Prescribing and dispensing restrictions
The initial prescription and dispensing of Erivedge should occur within 7 days of a negative pregnancy test. Prescription should be limited to 28 days treatment. Continuation requires a new prescription.

Contraception
These women must be able to comply with recommended contraceptive measures (see SmPC section 4.5 and 4.6), including one highly effective method and a barrier method during treatment and **for 24 months** after the final dose.

During treatment with Erivedge

Women of childbearing potential

Pregnancy testing
In these women, a pregnancy test should be conducted by a healthcare professional monthly during treatment. Pregnancy tests should have a minimum sensitivity of 25 mIU/mL hCG or as per local availability. Patients who present with amenorrhoea during treatment should continue pregnancy testing.

Contraception
These women must adhere to recommendations of contraception (see SmPC), during treatment and for 24 months after the final dose. In these women whose periods are irregular or have stopped, they must follow all the advice on recommended contraception.

In case of pregnancy or missed menstrual periods
A patient who becomes pregnant, misses a menstrual period, or suspects for any reason that she may be pregnant must notify her treating healthcare professional immediately. Persistent lack of menses during treatment should be assumed to indicate a pregnancy until medically evaluated and confirmed. In cases of pregnancy or suspicion of pregnancy, treatment must be stopped immediately.

Breastfeeding
The extent to which Erivedge is excreted in breast milk is not known. However, because of its potential to cause serious developmental defects, women must not breastfeed while taking Erivedge and for 24 months after the final dose.

Men
Erivedge is contained in semen. To avoid potential foetal exposure during pregnancy, male patients must always use a condom (with spermicide, if available), even after a vasectomy, when having sex with a female partner while taking Erivedge and for 2 months after the final dose.

All patients
Blood donation

Patients should not donate blood while taking Erivedge and for 24 months after the final dose.

Call for Reporting

▼This medicinal product is subject to additional monitoring. Reporting suspected adverse events after authorisation the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse reaction should also be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt.

Adverse events should also be reported to Roche Products Ltd. Please contact Roche Drug Safety Centre by emailing welwyn.uk_dsc@roche.com or calling +44(0)1707 367554.

For further detailed information about the PPP, we have enclosed the following:

- Healthcare Professional Brochure (including Reminder Card)
- Patient Information Brochure (including Reminder Card)
- Verification of Counselling Form
- Summary of Product Characteristics (SmPC) & Patient Information Leaflet (PIL)

Further Information:
Should you have any questions regarding the use of Erivedge, please feel free to contact Roche Medical Information UK on +44 (0) 800 328 1629 or email at medinfo.uk@roche.com.

Yours faithfully,

Dr. Daniel Thurley MA MB B Chir MRCP FFPM
UK Medical Director
Roche Products Ltd