9 September 2013.

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

Dear Healthcare Professional,

This letter is sent in agreement with the European Medicines Agency and the Irish Medicines Board 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 physician 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 should 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 Patient Reminder Card that summarise the measures of the PPP to be followed**
  - **that all patients complete and sign a Verification of Counselling Form (VCF).**

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.

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Before starting treatment with Erivedge

Women of childbearing potential (for the definition of Women of childbearing potential please refer to Section 4.4 of the Erivedge Summary of Product Characteristics (SmPC) or the Erivedge Healthcare Professional Information Brochure)

Pregnancy testing

In these women, a pregnancy test conducted by a healthcare professional 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 effective 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 effective 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 physician immediately. Persistent lack of menses during treatment should be assumed to indicate a pregnancy until medically evaluated and confirmed. In case 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
Erivedge is subject to additional monitoring. To reflect this, an inverted black triangle (▼) appears in the Erivedge SmPC and Package Leaflet. The purpose of the symbol is to actively encourage healthcare professionals and patients to report any suspected adverse reactions observed with the medicine. This will allow quick identification of new safety information.
Healthcare professionals should report any pregnancy and also all adverse events suspected to be associated with the use of Erivedge to the Drug Surveillance Centre at Roche Products (Ireland) Limited, 3004 Lake Drive, Citywest, Naas Road, Dublin 24 by mail, telephone (01 4690700), fax (01 4690793) or email (Ireland.drug_surveillance_centre@roche.com). Alternatively, suspected adverse reactions should be reported to the IMB using a Yellow Card obtained either from the IMB, or electronically via the website at www.imb.ie. Alternatively adverse reactions can be reported by calling on 01-6764971.

Erivedge PPP - Educational material
In order to assist healthcare professionals and patients to avoid embryonic and foetal exposure to Erivedge, Roche are providing educational materials (Erivedge PPP) which are enclosed with this letter to reinforce the potential risks associated with the use of Erivedge.
For further detailed information about the PPP please see the Erivedge Healthcare Professional Information Brochure [enclosed] or the Erivedge SmPC [enclosed and also available at www.medicines.ie].

For further information regarding the use of Erivedge or if you require additional copies of any of the Erivedge educational materials please contact Medical Information at Roche Products (Ireland) Limited, 3004 Lake Drive, Citywest, Naas Road, Dublin 24 by mail, telephone (01 4690700), fax (01 4690791) or email (Ireland.druginfo@roche.com).

Yours sincerely

Dr. Maria Luz Amador
Medical Director

Enclosures

1. Erivedge (vismodegib) Healthcare Professional Information Brochure (Version 1.0 July 2013)
2. Erivedge (vismodegib) Healthcare Professional Reminder Card (Version 1.0 July 2013)
3. Erivedge (vismodegib) Verification of Counselling Form (Version 1.0 July 2013)
4. Erivedge (vismodegib) Patient Information Brochure (Version 1.0 July 2013)
5. Erivedge (vismodegib) Patient Reminder Card (Version 1.0 July 2013)
6. Erivedge Summary of Product Characteristics (dated 12 July 2013)
7. Roche Pregnancy Report Form (Version 1.0 July 2013)