Roche Products (Ireland) Limited
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December 13th 2013

Subject: ***Severe skin reactions associated with Capecitabine (Xeloda®)***

Dear Healthcare Provider,

Roche Products (Ireland) Limited in agreement with the European Medicines Agency and the Irish Medicines Board would like to inform you of the following safety information regarding the use of Xeloda® (capecitabine):

Summary

- Very rare cases of severe skin reactions such as Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), in some cases with fatal outcome, have been reported during treatment with Xeloda.
- Healthcare professionals should be alert to the possibility of such reactions, and should stop treatment with Xeloda promptly if they occur.
- Xeloda should be permanently discontinued in patients who experience a severe skin reaction during treatment.
- Patients should be informed of the possibility of such reactions and told to seek urgent medical advice should any symptoms of severe skin reactions occur.

Roche is working closely with health authorities to update the product information.

Further information on the safety concern

Severe skin reactions such as SJS and TEN, in some cases with a fatal outcome, have been reported during treatment with Xeloda. The frequency of such reactions is estimated as very rare (less than 1 in 10,000).

TEN and SJS are characterised by generalised tender erythematous maculae progressing to blisters and denudation and often preceded by photophobia, symptoms of upper respiratory tract infection and fever. Severe skin reactions, especially SJS and TEN, are associated with significant morbidity and mortality. These may be reduced in patients where the suspect drug is stopped early compared to those where the suspect drug is carried on after the development of the blisters. Healthcare providers should therefore be aware of the possibility of such reactions during Xeloda treatment, and ensure prompt action and treatment, including discontinuation of Xeloda, should they occur.

Other skin reactions seen with Xeloda include

(Xeloda monotherapy): Palmar-plantar erythrodysaesthesia (hand-foot syndrome) and dermatitis occurs very commonly (≥ 10%) with Xeloda. Rash, alopecia, erythema and dry skin are common reactions with Xeloda. Pruritus, localised exfoliation, skin hyperpigmentation, photosensitivity reactions and radiation recall syndromes have also been seen with Xeloda treatment.

Therapeutic indications

Xeloda® is indicated for

- Xeloda is indicated for the adjuvant treatment of patients following surgery of stage III (Dukes' stage C) colon cancer
- Xeloda is indicated for the treatment of metastatic colorectal cancer
- Xeloda is indicated for first-line treatment of advanced gastric cancer in combination with a platinum-based regimen
- Xeloda in combination with docetaxel is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of cytotoxic chemotherapy. Previous therapy should have included an anthracycline. Xeloda is also indicated as monotherapy for the treatment of patients with locally advanced or metastatic breast cancer after failure of taxanes and an anthracycline-containing chemotherapy regimen or for whom further anthracycline therapy is not indicated.

Further information

Full prescribing and adverse event information for Xeloda® can be found in the currently authorized product information available via www.medicines.ie.

Please distribute this communication further within your team.

Call for reporting

Health care professionals should report any serious adverse events suspected to be associated with the use of Xeloda to the Roche Drug Surveillance Centre 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 Irish Medicines Board (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 to the IMB by calling (01) 6764971.

Company contact point

Should you have any questions or require additional information regarding the use of Xeloda (capecitabine) please feel free to contact Roche Medical Information by mail, telephone (01 4690700), fax (01 4690791) or email (ireland.druginfo@roche.com).

Annexes:

The Xeloda Summary of Product Characteristics (SmPC) is currently being updated with the following text which will be available shortly on www.medicines.ie:

4.4 Special warnings and precautions for use

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Severe skin reactions: Xeloda can induce severe skin reactions such as Stevens-Johnson syndrome and Toxic Epidermal Necrolysis. Xeloda should be permanently discontinued in patients who experience a severe skin reaction during treatment.

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4.8 Undesirable effects

Post-Marketing Experience:

The following additional serious adverse reactions have been identified during post-marketing exposure:

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Severe Skin Reactions (see section 4.4)

Very rare: Severe skin reactions such as Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis.

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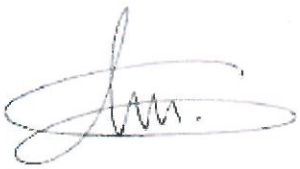
Yours sincerely,



Dr. Maria Luz Amador
Medical Director