03 December 2013

Increased risk of serious bleeding in Unstable Angina (UA)/NSTEMI patients when EFIENT® is administered prior to diagnostic coronary angiography.

Dear Healthcare Professional,

Eli Lilly and Company (Lilly), in agreement with the European Medicines Agency and the Irish Medicines Board, wish to inform you of the following recommendation concerning the use of EFIENT (prasugrel), an antiplatelet agent indicated for treatment of acute coronary syndrome (ACS) in patients undergoing PCI:

> **In UA/NSTEMI patients, when coronary angiography is performed within 48 hours after admission, the loading dose of EFIENT should only be given at the time of PCI in order to minimize the risk of bleeding.**

This is based on the outcome of a recently completed clinical study in NSTEMI patients[1] who were scheduled to undergo coronary angiography within 2 to 48 hours after randomization. The study compared the effects of giving an initial 30 mg loading dose of prasugel prior to coronary angiography (4 hours on average), followed by an additional dose of 30 mg at the time of PCI with the effects of giving a full 60 mg loading dose at the time of PCI. The results showed an increased risk of bleeding with the use of an initial loading dose prior to coronary angiography, followed by an additional dose at the time of PCI, compared with a single prasugrel loading dose at the time of PCI. No differences in efficacy between the two dosing regimens have been found.

Further information on the safety concern

ACCOAST was a 30-day study in 4033 patients with NSTEMI with elevated troponin who were scheduled to undergo coronary angiography followed by PCI within 2 to 48 hours after randomization. Subjects who received a prasugrel 30 mg loading dose on average 4 hours prior to coronary angiography followed by a 30 mg loading dose at the time of PCI (n=2037) had an increased risk of non-CABG peri-procedural bleeding and no additional benefit compared to patients receiving a 60 mg loading dose at the time of PCI (n=1996). Specifically, the frequency of the composite endpoint of cardiovascular death, myocardial infarction, stroke, urgent revascularization, or the use of glycoprotein (GP) IIb/IIIa inhibitors as bailout therapy within 7 days after randomization was not significantly reduced in patients

[1] The "ACCOAST" study, entitled, *A Comparison of Prasugrel at the Time of Percutaneous Coronary Intervention Or as Pre-treatment at the Time of Diagnosis in Patients with Non-ST-Elevation Myocardial Infarction.*

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who received prasugrel prior to coronary angiography when compared with patients who received the full loading dose of prasugrel at the time of PCI. In addition, the rate of the key safety objective for all TIMI major bleeding (CABG and non-CABG events) through 7 days from randomization in all treated subjects was significantly higher in subjects who received prasugrel prior to coronary angiography versus patients who received the full loading dose of prasugrel at the time of PCI.

The information is being sent in agreement with the European Medicines Agency and the Irish Medicines Board (IMB).

Reporting Adverse Events

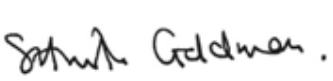
To report adverse events among patients taking EFIENT, please contact Lilly at: 01 6614377.

Alternatively, adverse event information may be reported to the IMB:

Phone: 01 6764971
Facsimile: 01 6762517
Mail: Pharmacovigilance Section, Irish Medicines Board, Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2, Ireland
Online: www.imb.ie
Email: imbpharmacovigilance@imb.ie

Please contact Lilly at: 01 6614377, if you have any questions about the information in this letter or the safe and effective use of EFIENT.

Yours sincerely,



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Annexed: revised SmPC with changes highlighted.
Please note, the revised SmPC attached is the Efient 10 mg strength only.
The same changes will apply to the Efient 5mg strength. It is anticipated that the revised SmPC will be available on relevant electronic compendia from late January 2014.