



IRISH MEDICINES BOARD

28 July 2010

ROSIGLITAZONE (AVANDIA/ AVANDAMET) AND CARDIOVASCULAR RISK

Dear Healthcare Professional,

Further to previous regulatory updates on cardiovascular risk with rosiglitazone, the IMB is writing to reinforce existing recommendations about the use of rosiglitazone (Avandia/ Avandamet) in the treatment of diabetes and to inform you that new data concerning rosiglitazone and cardiovascular risk are under evaluation at EU level.

Rosiglitazone is a second line treatment in type II diabetes, which should only be used when other treatments have either failed or are unsuitable for a patient.

Use of Avandia (rosiglitazone) has been contraindicated in patients with heart failure or a history of heart failure since its first authorisation in July 2000. A combination of rosiglitazone with metformin was subsequently approved as Avandamet and this is also contraindicated in patients with heart failure or a history of heart failure. Since authorisation, use of these medicines has been further restricted several times by the introduction of new warnings and contraindications on their use in patients with heart problems.

The European Committee on Medicinal Products for Human Use (CHMP) is currently reviewing rosiglitazone to determine the impact of new published data on the risk of cardiovascular problems on the benefit- risk profile of these medicines. The new data include two published studies examining rosiglitazone^{1,2} and newly available information from the US Food and Drug Administration which raise concern regarding the cardiovascular risk with rosiglitazone compared with both placebo and pioglitazone. The new studies involved a large number of diabetic patients and add to the accumulating evidence from different global data sources and different types of studies on rosiglitazone and cardiovascular risk.

Pending the outcome of the CHMP review, prescribers should review patients in line with the recommended monitoring to ensure that all contraindications and warnings are strictly observed. Prior to initiation of new treatment and in the ongoing monitoring of patients, doctors should pay particular attention to the following:

Bord Leigheasra na hÉireann

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Cardiovascular Warnings and Contraindications:

- Rosiglitazone must not be used in patients with current or previous heart failure and in patients with acute coronary syndrome
- The use of rosiglitazone is not recommended in patients with ischaemic heart disease or peripheral arterial disease.
- Rosiglitazone and insulin should only be used together in exceptional cases and under close supervision

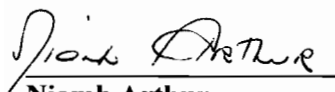
Monitoring requirements

- Prescribers are required to monitor patients for signs and symptoms of adverse reactions relating to fluid retention, including weight gain and heart failure.
- Increased monitoring of the patient is recommended if rosiglitazone is used in combination with metformin and insulin.
- Rosiglitazone should be discontinued if any deterioration in cardiac status occurs.

The full prescribing information for Avandia/Avandamet is available on the EMA website http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000268/human_med_000662.jsp&url=menus/medicines/medicines.jsp&mid=WC0b01ac058001d124 .

It is anticipated that the Europe-wide review of available data on the risk and benefits of rosiglitazone will be completed by September 2010. The IMB is actively involved in this review, through its membership of the relevant EU Committees and will communicate the outcome, when available.

Yours sincerely,



Niamh Arthur,
Pharmacovigilance Manager

References:

1. Graham DJ et al. Risk of acute myocardial infarction, stroke, heart failure, and death in elderly Medicare patients treated with rosiglitazone or pioglitazone. JAMA doi:10.1001/jama.2010.920.
2. Nissen SE et al. Rosiglitazone revisited. An updated meta analysis of risk for myocardial infarction and cardiovascular mortality. Arch Intern Med doi:10.1001/archinternmed.2010.207