24th September 2010

Circular No. P11/2010

Dear Healthcare Professional,

Re: European Medicines Agency recommends suspension of Avandia, Avandamet and Avaglim

The European Medicines Agency has recommended the suspension of the marketing authorisations for the rosiglitazone-containing anti-diabetes medicines Avandia, Avandamet and Avaglim. These medicines will stop being available in Malta as well as the rest of Europe within the next few months.

- **Prescribers are advised not to issue any new or repeat prescriptions of rosiglitazone-containing medicines**
- **Prescribers are advised to review currently treated patients and switch them to suitable alternative treatment**
- **Pharmacists are advised to refer patients to their doctor for advice on their treatment**
- **Patients are advised to make an appointment to discuss their treatment and not to stop taking rosiglitazone without consulting their doctor.**

The current review of rosiglitazone was initiated on 9 July 2010 following the availability of new studies questioning the cardiovascular safety of the medicine. (See below for references)

Since its first authorisation, rosiglitazone has been recognized to be associated with fluid retention and increased risk of heart failure and its cardiovascular safety has always been kept under close review. Consequently, the use of rosiglitazone was restricted to a second-line treatment and contra-indicated in patients with heart failure or a history of heart failure when it was first granted a marketing authorisation as Avandia in 2000.

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Data from clinical trials, observational studies and meta-analyses of existing studies that have become available over the last three years have suggested a possibly increased risk of ischaemic heart disease associated with the use of rosiglitazone. Further restrictions on the use of these medicines in patients with ischaemic heart disease were introduced.

The availability of recent studies has added to the knowledge about rosiglitazone and overall, the accumulated data support an increased cardiovascular risk of rosiglitazone. In view of the restrictions already in place on the use of rosiglitazone, the Committee could not identify additional measures that would reduce the cardiovascular risk. The Committee therefore concluded that the benefits of rosiglitazone no longer outweigh its risks and recommended the suspension of the marketing authorisation of the medicines.

The suspension will remain in place unless the marketing authorisation holder can provide convincing data to identify a group of patients in whom the benefits of the medicines outweigh their risks.

The Committee's recommendation has now been forwarded to the European Commission for the adoption of a legally binding decision.

References for the studies are as follows:

- **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.
- **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.

1. The Medicines Authority has participated in the discussions held at the EMA and is in agreement with the full **press release** issued by the EMA, attached here for your perusal. A **question-and-answer** document with more information about the outcome of this assessment is also available.

Healthcare professionals are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

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