Direct Healthcare Professional Communication

3 October 2018

Sildenafil (Revatio and Viagra) should not be used to treat intrauterine growth restriction

Dear Healthcare professional,
Pfizer, in agreement with the European Medicines Agency (EMA) and Malta Medicines Authority, would like to inform you of the following:

Summary

- **The STRIDER clinical trial, which was studying sildenafil for treating intrauterine growth restriction (IUGR), has been prematurely discontinued due to a higher incidence of persistent pulmonary hypertension of the newborn (PPHN) and overall neonatal death in the sildenafil arm of the study.**
- **Sildenafil is not approved for IUGR.**
- **Revatio and Viagra should not be used for treating IUGR.**
- **Revatio and Viagra should only be used in accordance with the current product information.**

Background on the safety concern
Sildenafil is the active substance of the medicinal products Revatio and Viagra.
Revatio is approved for the treatment of adults and children aged 1 to 17 years with pulmonary arterial hypertension (PAH). The approved product information for Revatio states that use in pregnancy is not recommended and the medicine should only be used when strictly necessary in pregnant women for the treatment of PAH.
Viagra is used in the treatment of men with erectile dysfunction. It is not indicated for use in women.

The Dutch STRIDER (Sildenafil TheRapy In Dismal prognosis Early-onset intrauterine growth Restriction) study is an independent clinical trial. Pregnant women were randomised to generic sildenafil or placebo. Sildenafil was given in a dose of 25 mg three times a day to pregnant women for the treatment of severe intrauterine (fetal) growth restriction (IUGR). This dose is higher than the recommended doses for both Viagra and Revatio. The study was one of 5 independent non-Pfizer sponsored studies by an international collaboration investigating the use of sildenafil for this unapproved use. The Dutch STRIDER study was prematurely discontinued due to a serious concern that the use of sildenafil in IUGR may be harming newborn infants. The investigators' interim analysis showed an imbalance in the incidence of persistent pulmonary hypertension of the newborn (PPHN) (sildenafil 17/64 (26.6%), placebo 3/58 (5.2%)) and overall neonatal death prior to discharge (sildenafil 19/71 (26.8%), placebo 9/63 (14.3%)) between treatment arms. Details of the interim analysis are not yet available and the analysis by the STRIDER consortium of studies is awaited.

Call for reporting
Healthcare professionals are reminded to report suspected adverse reactions associated with the use of Revatio & Viagra in accordance with the national spontaneous system. Any suspected adverse reactions and medication errors can be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Malta Medicines Authority Post-licensing, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta or sent by email to postlicensing.medicinesauthority@gov.mt

Company contact point
Company contact point for additional information:

Product name	Company	Email	Phone	Fax
Revatio Viagra	Pfizer Hellas S.A, Greece Local representative: V.J. Salomone Pharma Ltd.	GRC.AEReporting@pfizer.com or medical.information@pfizer.com Local contact: regvjsp@vjsalomone.com	+30 210 6785800 Local number: +356 99644126 +356 21220174	+30 210 8199096 Local number: +356 21243026

Annexes

- Detailed information on Revatio is available on the European Medicines Agency web site: https://www.ema.europa.eu/documents/product-information/revatio-epar-product-information_en.pdf
- Detailed information on Viagra is available on the European Medicines Agency web site: https://www.ema.europa.eu/documents/product-information/viagra-epar-product-information_en.pdf

Yours sincerely,

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Medical Director
Greece, Cyprus and Malta