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Worldwide Biopharmaceutical Businesses

Direct Healthcare Professional Communication

15th 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 the Medicines and Healthcare product Regulatory Agency (MHRA), 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.

Registered in England: No 526209
Registered Office: Ramsgate Road
Sandwich, Kent CT13 9NJ, UK

Call for reporting
You can assist us with monitoring the safety of Revatio and Viagra by reporting suspected adverse reactions. Suspected adverse drug reactions (ADRs) should be reported to the Medicines and Healthcare product Regulatory Agency (MHRA) through the Yellow Card Scheme online at www.mhra.gov.uk/yellowcard.

Alternatively, prepaid Yellow Cards for reporting are available:

- upon request by mail: "FREEPOST YELLOW CARD"
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- Or by electronic download through the Yellow Card section of the MHRA website

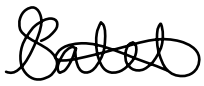
Suspected adverse drug reactions may also be reported to Pfizer Medical Information on 01304 616161.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates.

Company contact point
If you have any questions about this letter or for more information about Revatio and Viagra, please contact Pfizer Medical Information at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS or Telephone: 01304 616 161

Annexes
Link for Health Care Professionals to access Summary of Product Characteristics (SPC) in local language – https://www.medicines.org.uk/emc/

Yours sincerely,



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