DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION (DHPC)

28-09-2020

Modafinil: potential risk of congenital malformations when administered during pregnancy

Dear Healthcare Professional,

Bluefish Pharmaceuticals is in agreement with the Health Products Regulatory Authority (HPRA), to send this letter to inform you of important new safety information regarding modafinil exposure during pregnancy which has arisen following review of a signal of major congenital anomaly identified following review of data ascertained from the Nuvigil® and Provigil® pregnancy registry (NCT01792583; clinicaltrials.gov).

This information was already shared with relevant Irish healthcare professionals in 2019 by other marketing authorisation holders. Since Bluefish is now planning to launch the product, the letter is being redistributed.

SUMMARY

- **Based on post-marketing reports from the US Nuvigil® and Provigil® Pregnancy Registry and other spontaneous sources, the use of modafinil during pregnancy is suspected to cause congenital malformations.**
- **Modafinil should not be used during pregnancy**
- **Women of childbearing potential must use effective contraception during treatment with, and for 2 months after stopping, modafinil;**
- **You must ensure that all female patients of childbearing potential are informed of and fully understand;**
    - **The potential risk to a foetus associated with modafinil use during pregnancy;**
    - **That modafinil should not be used during pregnancy;**
    - **The need to use effective contraception during treatment with and for 2 months after stopping modafinil. As modafinil may reduce the effectiveness of oral contraception, alternative or concomitant methods of contraception are required.**
    - **The need to discuss other treatment options with their doctor if planning a pregnancy before stopping contraception**

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- **Non-pharmacological treatment options including behaviour modifying measures, sleep hygiene, and scheduled daytime naps should be preferred during pregnancy**.

BACKGROUND ON THE SAFETY CONCERN

The Nuvigil® and Provigil® registry is a prospective, observational study in the United States (US) to characterise the pregnancy and foetal outcomes associated with modafinil/armodafanil exposure from six weeks prior to conception and/or during pregnancy. Major birth defects are the primary endpoint of the registry and as a result major structural and functional birth defects identified in the perinatal period through 12 months of life are collected and classified. The Pregnancy Registry Advisory Committee (RAC) adjudicates cases within the registry and provides annual reports.

Reports of major congenital malformations including congenital heart defects, hypospadias and orofacial clefts for which causal relation with modafinil is considered possible, were received from the Registry and other spontaneous sources. Based on the interim data ascertained from the 2018 Annual Registry report the rate of major congenital malformations was approximately 15% compared to 3%1 in the general population. Modafinil should therefore not be used in women who are pregnant and should not be used in women who may become pregnant unless they are using effective contraception.

In addition to the findings from the registry, studies in animals have shown reproductive toxicity.

FURTHER INFORMATION ON THE SAFETY CONCERN AND RECOMMENDATIONS

- Modafinil is indicated in adults for the treatment of excessive sleepiness associated with narcolepsy with or without cataplexy.

-Modafinil Bluefish product information includes this information.

CALL FOR REPORTING

Healthcare professionals are asked to report any suspected adverse events to the Health Products Regulatory Authority, via HPRA Pharmacovigilance, website: www.hpra.ie.

Adverse events may also be reported to the Bluefish Pharmaceuticals as per the contact details provided in table 1.

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COMPANY CONTACT POINT

If you have any questions or require additional information, please contact the relevant Bluefish Pharmaceuticals as below:

Table 1

Company	Product	Email	Phone
Bluefish Pharmaceuticals	Modafinil Bluefish	drugreaction@bluefishpharma.com	+353-14687672 +353-867816453

Further information is also located on the medicines information section of the HPRA website: www.hpra.ie

Yours Sincerely

Digitally signed by Lena Sundqvist
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Date: 2020.08.10 14:21:06 +02'00'

Lena Sundqvist
Deputy QPPV & Head of Local Drug Safety Officers
Bluefish Pharmaceuticals

Reference 1) Canfield MA, Honein MA, Yuskiv N, et al. National estimates and race/ethnic-specific variation of selected birth defects in the United States, 1999–2001. Birth Defects Research (Part A) 2006; 76:747–56

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