

8<sup>th</sup> January 2020

## **Direct Healthcare Professional Communication (DHPC)**

### **Modafinil: potential risk of congenital malformations during pregnancy**

Dear xxxxxxxxxxxx,

Marketing Authorisation Holders of generic medicines containing modafinil, in agreement with the UK regulator MHRA, inform you of the following safety information:

#### **SUMMARY**

- **Based on post-marketing reports from the US Nuvigil and Provigil Pregnancy Registry and other spontaneous sources, use of modafinil during pregnancy is suspected to cause congenital malformations (including congenital heart defects, hypospadias, and orofacial clefts)**
- **Of the 78 prospective pregnancy cases identified within the registry, 61 cases reported a live birth outcome, 9 of which presented with major congenital anomalies.**
- **Modafinil should not be used during pregnancy.**
- **Alternative treatment options should be used during pregnancy, including behaviour modifying measures, sleep hygiene, and scheduled daytime naps**
- **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 about and fully understand:**

- a) The potential risk to a foetus if modafinil is used during pregnancy
- b) That modafinil should not be used during pregnancy
- c) The need to use effective contraception during treatment with, and for 2 months after stopping, modafinil.
- d) As modafinil may reduce the effectiveness of oral contraception, alternative or additional methods of contraception are required.
- e) The need to discuss other treatment options with their doctor if planning a pregnancy before stopping contraception

## **FURTHER INFORMATION ON THE SAFETY CONCERN**

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

The Nuvigil® and Provigil® Registry (NCT01792583; ClinicalTrials.gov) is a prospective, observational study in the United States (US) to characterise the pregnancy and foetal outcomes associated with modafinil/armodafinil 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 up to 12 months of life are collected and classified.

Reports of major congenital malformations including congenital heart defects, hypospadias and orofacial clefts for which a causal relation with modafinil is considered possible, were received from the registry and other spontaneous sources.

**Based on the interim data from the 2018 Annual Registry report, the overall rate of major congenital malformations was approximately 15% compared to 3% in the general population. The prevalence of cardiac anomalies 4.92 % is also higher than reported in the general population (1.0 %).**

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

## **Reporting of side effects**

Please continue to report suspected side effects to the MHRA through the Yellow Card Scheme. Please report:

- all suspected side effects that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- all suspected side effects associated with new drugs and vaccines identified by the black triangle ▼
- It is easiest and quickest to report side effects online via the Yellow Cards website - <https://yellowcard.mhra.gov.uk/> or via the Yellow Card app available from the Apple App Store or Google Play Store.  
Alternatively, prepaid Yellow Cards for reporting are available by writing to FREEPOST YELLOW CARD (no other address details necessary); by emailing

yellowcard@mhra.gov.uk; 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 downloading and printing a form from the Yellow Card website.

This letter is being provided by the group of generic companies listed below, who are Marketing Authorisation holders for these medicines. If you require additional information, please contact the individual company.



Paul Fleming  
Technical Director



<b>Company</b>	<b>Medical Information contact details</b>
Chanelle Medical	<a href="mailto:chanelle@medinformation.co.uk">chanelle@medinformation.co.uk</a> Telephone: 0870 1923 283
Crescent Pharma Ltd	<a href="mailto:info@crescentpharma.com">info@crescentpharma.com</a> Telephone: 0125 6772 730
Drugsrus Limited / Dawa Limited	<a href="mailto:pv@drugsrus.co.uk">pv@drugsrus.co.uk</a> Telephone: 0208 4233 800
Milpharm Limited	<a href="mailto:medinfo@aurobindo.com">medinfo@aurobindo.com</a> Telephone: 0208 845 8811
Morningside Healthcare Limited	<a href="mailto:medicalenquiry@Morningsidehealthcare.com">medicalenquiry@Morningsidehealthcare.com</a> Telephone: 0345 4592 137
Mylan	<a href="mailto:info.uk@mylan.co.uk">info.uk@mylan.co.uk</a> Telephone: 0174 8828 888
Teva UK Limited	<a href="mailto:medinfo@tevauk.com">medinfo@tevauk.com</a> Telephone: 0207 5407 117
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