



Ireland

Teva Pharmaceuticals Ireland

www.teva.ie

Direct Healthcare Professional Communication (DHPC)

7th June 2019

Modafinil: potential risk of congenital malformations when administered during pregnancy

Dear Healthcare Professional,

Marketing Authorisation Holders of products containing modafinil (see Table 1), in agreement with the European Medicines Agency (EMA) and Health Products Regulatory Authority (HPRA), 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).

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**
- **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/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 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% 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.

Date of Preparation: May 2019. Job code: IE/MED/19/0010

Teva Pharmaceuticals Ireland

Digital Office Centre Swords, Suite 101 - 103, Balheary Demense, Balheary Road, Swords, Co Dublin, K67E5A0, Ireland
Telephone: 1800 201 7000 | Tel: +353 51 321 740 | Fax: +353 (0)42 935 1516

Teva Pharmaceuticals Ireland is a registered business name of Norton (Waterford) Limited.
Registered Office is Unit 301, Industrial Park, Cork Road, Waterford, Republic of Ireland.

Norton (Waterford) Limited is a private company limited by shares registered in Ireland under registration number 100363
Directors: Andy Crowley, Ray Finnegan, Dean Cooper (UK)

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.
- The product information for these products will be amended to reflect our current understanding of the available evidence.

CALL FOR REPORTING

Healthcare professionals are asked to report any suspected adverse events to the Health Products Regulatory Authority, via **HPRA Pharmacovigilance, Earlsfort Terrace, IRL-Dublin 2**; Tel: **+35316764971**; Fax: **+35316762517**. Website: **www.hpra.ie**; Email: **medsafety@hpra.ie**. Adverse events may also be reported to the relevant Marketing Authorisation Holders as per the contact details provided in table 1.

COMPANY CONTACT POINT

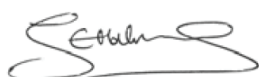
If you have any questions or require additional information please contact the relevant Marketing Authorisation Holders as below:

TABLE 1

Company	Product name	Email	Phone
Teva Pharmaceuticals Ireland	Provigil 100 mg Tablets Provigil 200 mg Tablets	Suspected adverse reactions: safety.ireland@teva.ie Additional information: medinfo@tevauk.com	Additional Information/Suspected adverse reactions: +44 (0)207 540 7117
Clonmel Healthcare Ltd.	Prosentio 100 mg Tablets Prosentio 200 mg Tablets	Additional Information / Suspected adverse reactions: medicalinformation@clonmel-health.ie	Additional Information / Suspected adverse reactions: +353 52 617777
Fannin Limited	Modafinil 100mg Tablets Modafinil 200mg Tablets	Additional Information / Suspected adverse reactions: medical@dccvital.com	Additional Information / Suspected adverse reactions: 086-8394447 09066-61109

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

Yours Sincerely,



John Holmes
UK & Ireland Director Medical Services

Signed on behalf of the Marketing Authorisation Holders listed in table 1

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

Date of Preparation: May 2019. Job code: IE/MED/19/0010

Teva Pharmaceuticals Ireland

Digital Office Centre Swords, Suite 101 - 103, Balheary Demense, Balheary Road, Swords, Co Dublin, K67E5A0, Ireland
Telephone: 1800 201 7000 | Tel: +353 51 321 740 | Fax: +353 (0)42 935 1516

Teva Pharmaceuticals Ireland is a registered business name of Norton (Waterford) Limited.
Registered Office is Unit 301, Industrial Park, Cork Road, Waterford, Republic of Ireland.

Norton (Waterford) Limited is a private company limited by shares registered in Ireland under registration number 100363
Directors: Andy Crowley, Ray Finnegan, Dean Cooper (UK)