Summary of risk management plan for Modasomil® (Modafinil)

Teva Pharma AG
Kirschgartenstrasse 14
4010 Basel

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Disclaimer

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risk as well as to prevent or minimize them.

The RMP summary of Modasomil® is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Modasomil® in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedicinfo.ch) approved and authorized by Swissmedic. Teva Pharma AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Modasomil®.

Summary of Risk Management Plan for Modasomil, Vigil, Modiodal, Provigil (modafinil)

This is a summary of the risk management plan (RMP) for Modasomil, Vigil, Modiodal, Provigil (modafinil) (herein after also referred to as Modafinil). The RMP details important risks of Modafinil, how these risks can be minimised, and how more information will be obtained about Modafinil's risks and uncertainties (missing information).

Modafinil's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Modafinil should be used.

Important new concerns or changes to the current ones will be included in updates of Modafinil's RMP.

I. The Medicine and What It is used for

Modasomil, Vigil, Modiodal, Provigil (modafinil) is authorised for the treatment of excessive sleepiness associated with narcolepsy with or without cataplexy. It contains Modafinil as the active substance and it is given orally.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Modafinil, together with measures to minimise such risks and the proposed studies for learning more about Modafinil’s risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine’s legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Modafinil, these measures are supplemented with *additional risk minimisation measure* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A List of Important Risks and Missing Information

Important risks of Modafinil are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Modafinil. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this

association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Table 1: Summary of Safety Concerns

List of important risks and missing information	
Important identified risks	• None
Important potential risks	• Misuse, abuse and diversion • Teratogenicity
Missing information	• None

II.B Summary of Important Risks

Table 2: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Important potential risk: Teratogenicity	
Evidence for linking the risk to the medicine	Developmental toxicity (based on decreased foetal body weight and foetal variations) has been noticed in animal studies. Based on human experience from a pregnancy registry and spontaneous reporting modafinil is suspected to cause congenital malformations including congenital heart defects, hypospadias and orofacial clefts when administered during pregnancy.
Risk factors and risk groups	Women who are pregnant or may become pregnant and who are not using effective contraception.
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4 and 4.6. PL section 2. Prescription only medicine. Additional risk minimisation measures DHPC.
Additional pharmacovigilance activities	Additional pharmacovigilance activities US Nuvigil and Provigil Pregnancy Registry Post Authorization Safety Study: Assessment of pregnancy outcomes in women exposed to modafinil/armodafinil: Pregnancy database study.

II.C Post-Authorisation Development Plan

II.C.1 Studies Which Are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Modasomil, Vigil, Modiodal, Provigil (modafinil).

II.C.2 Other Studies in Post-Authorisation Development Plan

US Nuvigil and Provigil Pregnancy Registry

Prospective, observational registry collecting data regarding Nuvigil/Provigil exposure during pregnancy and subsequent pregnancy and fetal outcomes.

Purpose of the study:

To systematically collect prospective and retrospective data on the effects of exposure during pregnancy, labour, and delivery in women of childbearing age.

Assessment of Pregnancy Outcomes in Women Exposed to Modafinil/Armodafinil: Pregnancy Database Study

Purpose of the study:

The objective of this study is to estimate the prevalence of pregnancy outcomes, including major congenital malformations (MCMs), spontaneous abortions, stillbirths, low birth weight and small for gestational-age births/intrauterine growth retardation/failure to thrive, in women exposed to modafinil/armodafinil during pregnancy, compared to an unexposed control cohort. Additional exploratory study objectives are to analyze MCMs by major organ group and to estimate the relative risk of MCMs.