VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Narcolepsy are sleep attacks that make people very sleepy or fall asleep in inappropriate situations (e.g. during conversations or during work). Over time, it can also reduce the attention span, lead to muscle weakness, hallucinations, broken sleep at night and non-sleep problems like overweight, anxiety and emotional problems.

Between 25 and 47 out of 100,000 people in Europe suffer from narcolepsy [2, 3]. There seem to be more people affected in Germany and in the UK than in other countries of Europe [2]. You are as likely to suffer from narcolepsy regardless of sex [4].
The exact cause of narcolepsy is unknown and there is no cure available [5].

VI.2.2 Summary of treatment benefits

There were 2 important (so called pivotal) clinical studies to find out how effective modafinil is in keeping people with narcolepsy awake [6, 7]. In both studies participants were randomized (meaning it was by chance, like rolling a die) to receive either modafinil or identical looking tablets made only out of sugar (placebo). Neither the patients nor the doctors knew during the study who received what (double-blind).
Both studies used the objective maintenance of wakefulness test (MWT) to measure whether modafinil helped patients to stay awake longer. For the MWT patients are asked to stay awake as long as they can at specific times of the day. Also, the studies had the doctors of the patients fill out a questionnaire to measure the patients' change in sleepiness, the so called Clinical Global Impressions scale for change of condition (CGI-C)
The studies showed that on average, patients suffering from narcolepsy could stay longer awake when taking modafinil.

In Study 301 [6], 96 patients were randomized to receive 200 mg modafinil a day, 95 patients to receive 400 mg a day and 95 patients to receive placebo. By MWT, patients receiving either dose of modafinil were on average able to stay awake 2.3 minutes longer at the end of the study than at the beginning, which was better than in patients given placebo.
In study 302 [7], 90 patients were randomized to receive 200 mg modafinil a day, 90 patients to receive 400 mg a day and 93 patients to receive placebo. By MWT, patients receiving 200 mg of modafinil were on average able to stay awake 2.0 minutes longer, patients receiving 400 mg 2.3 minutes, which was better than in patients given placebo.
In both studies, more than 2/3 of patients given modafinil showed improvement measured by the CGI-C.

These studies were conducted for ProVigil by Cephalon Inc. (now owned by Teva Pharmaceutical Industries) and not by Mylan.

VI.2.3 Unknowns relating to treatment benefits

Very little is known about the effect of modafinil in pregnant women, children and the elderly.

VI.2.4 Summary of safety concerns

Table 13 Part VI - Summary table of safety concerns

Important identified risks

Risk	What is known	Preventability
Serious skin reactions	Up to 1 in 100 people treated with modafinil may suffer from non-serious skin rashes. Serious rash requiring patients to stop using modafinil may occur within 1 to 5 weeks after start of the treatment. Serious skin reactions can mean blistering or peeling of the skin, ulcers in the moth, eyes noses or genitals. It might be necessary for patients to visit a hospital. Rare cases have led to the death of the patient.	Doctors should look for rash and other symptoms in their patients. Treatment should be stopped at the first signs of rash. A doctor should be contacted right away.
Allergic reactions (Hypersensitivity reactions)	Allergic (hypersensitivity) reactions are extremely rare, but may evolve to a serious allergic reaction that affects the entire body, which can be life-threatening (anaphylactic reaction). It is unknown how many patients taking modafinil could be affected. Such reactions are usually caused by extreme sensitivity to certain components of the tablet, such as glucose.	Patients with a known allergy to modafinil or any other components of the tablet, should not take it (contraindication). Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose

Risk	What is known	Preventability
	These reactions can be life-threatening and may require patients to go to a hospital. Signs of an allergic reaction can be rash, fever, red skin.	malabsorption should not take this medicine

Irregular heartbeat and high blood pressure (cardiovascular disorders)	Up to 1 in 100 treated with modafinil may develop irregular heartbeat or high blood pressure.	Patients with irregular heartbeat or high blood pressure should not take modafinil (contraindication). Doctors should carefully observe such patients. An electrocardiogram or ECG (a test to check for problems with the electrical activity of the heart) is recommended for all patients before given modafinil. Patients developing problems with the heart should stop taking modafinil.
Changes in mental health and wellbeing (Psychiatric disorders)	Depending on the exact reaction, up to 1 out of 10 patients taking modafinil can be affected (e.g. anxiety, abnormal thoughts, depression and confusion). Other reactions are less common (e.g. suicidal thoughts, aggression in up to 1 out of 100 patients taking modafinil).	Doctors should be careful in patients with previous mental health problems and should consider stopping modafinil when changes in mental health are seen.

Risk	**What is known**	**Preventability**
Side effects of the nervous system (Nervous system disorders)	More than 1 out of 10 patients taking modafinil may suffer from headache. Up to 1 out of 10 patients may develop other side effects of the nervous systems, e.g. dizziness, sleepiness and extreme tiredness and numbness of hands and feet.	Doctors should carefully observe patients and should consider stopping modafinil if symptoms are severe or persistent.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Use of modafinil in conditions not authorized (Off-label use)	Modafinil has been prescribed in the past by doctors for conditions it is not authorized for, e.g. sleepiness and fatigue in other conditions than narcolepsy. There is little information on what side-effects modafinil can have in patients with those other conditions, which is why use outside of the therapeutic indication it is authorised for is not recommended.
Misuse, abuse, diversion	Modafinil has been misused as a so-called 'lifestyle drug' to stimulate alertness and wakefulness in otherwise healthy persons. In studies it was shown that modafinil has a low risk of addiction, however it is not known if this risk increases if the drug is used over a longer period of time. Because modafinil has a stimulating effect, doctors should observe patients closely that have a history of alcohol, drug or illegal substance abuse.

Missing information

None.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet. The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No studies planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable.