VILAFINIL

(Modafinil) Tablets, for Oral Use

Comprehensive Medication Guide & Prescribing Information

Initial U.S. Approval of Modafinil: 1998 • Wakefulness-Promoting Agent • C-IV

IMPORTANT DISCLAIMER

This document is a comprehensive educational guide compiled in the style of an official medication package insert. It is based on publicly available FDA-approved labeling for modafinil (e.g., Provigil® and generics). Vilafinil is a brand name used for modafinil tablets manufactured by Centurion Laboratories. This is NOT a substitute for professional medical advice or the official product labeling. Modafinil is a controlled substance. Always consult a qualified healthcare provider.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VILAFINIL (modafinil) safely and effectively. See full prescribing information.

INDICATIONS AND USAGE

Vilafinil (modafinil) is a wakefulness-promoting agent indicated to improve wakefulness in adult patients with excessive sleepiness associated with:

- Narcolepsy
- Obstructive sleep apnea (OSA) — treats excessive sleepiness only; not a treatment for the underlying airway obstruction
- Shift work disorder (SWD)

DOSAGE AND ADMINISTRATION

- Narcolepsy or OSA: 200 mg once daily in the morning.
- SWD: 200 mg once daily, taken approximately 1 hour before the start of the work shift.
- Severe hepatic impairment: reduce to half the recommended dose (typically 100 mg daily).
- Geriatric patients: consider a lower dose.
- Doses up to 400 mg/day have been tolerated, but there is no consistent evidence of additional benefit beyond 200 mg/day.

DOSAGE FORMS AND STRENGTHS

Tablets: 100 mg and 200 mg (appearance and imprint may vary by manufacturer).

CONTRAINDICATIONS

Known hypersensitivity to modafinil or armodafinil.

WARNINGS AND PRECAUTIONS

- Serious rash, including Stevens-Johnson Syndrome: discontinue at the first sign of rash unless clearly not drug-related.
- Angioedema and anaphylaxis: discontinue if suspected.
- Multi-organ hypersensitivity reactions: discontinue if suspected.
- Persistent sleepiness: not a substitute for sleep; assess degree of sleepiness and advise against driving or hazardous activity if still sleepy.
- Psychiatric symptoms: use caution; discontinue if psychosis, mania, depression, or aggression develops.
- Known cardiovascular disease: consider increased monitoring.

ADVERSE REACTIONS

Most common (≥5%): headache, nausea, nervousness, rhinitis, diarrhea, back pain, anxiety, insomnia, dizziness, and dyspepsia.

DRUG INTERACTIONS

Modafinil may reduce the effectiveness of steroidal contraceptives. Alternative or concomitant methods of contraception are recommended during treatment and for one month after discontinuation. Modafinil can affect CYP3A4, CYP2C19, and other enzymes.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Vilafinil (modafinil) is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea (OSA), or shift work disorder (SWD).

Limitations of Use: In OSA, Vilafinil is indicated to treat excessive sleepiness and is not a treatment for the underlying obstruction. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximal effort to treat with CPAP for an adequate period of time should be made prior to initiating and during treatment with Vilafinil.

2 DOSAGE AND ADMINISTRATION

2.1 Narcolepsy and Obstructive Sleep Apnea

The recommended dosage is 200 mg taken orally once a day as a single dose in the morning. Doses up to 400 mg/day, given as a single dose, have been well tolerated, but there is no consistent evidence that this dose confers additional benefit beyond that of the 200 mg/day dose.

2.2 Shift Work Disorder

The recommended dosage is 200 mg taken orally once a day as a single dose approximately 1 hour prior to the start of the work shift.

2.3 Dosage in Severe Hepatic Impairment

In patients with severe hepatic impairment, the dose should be reduced to one-half of that recommended for patients with normal hepatic function (typically 100 mg daily).

2.4 Use in Geriatric Patients

Consideration should be given to the use of lower doses and close monitoring in geriatric patients.

Vilafinil may be taken with or without food.

3 DOSAGE FORMS AND STRENGTHS

Tablets containing 100 mg or 200 mg of modafinil. Color, shape, and imprint vary by manufacturer. Vilafinil is commonly supplied as 200 mg tablets.

4 CONTRAINDICATIONS

Vilafinil is contraindicated in patients with known hypersensitivity to modafinil or armodafinil or any inactive ingredients in the formulation.

5 WARNINGS AND PRECAUTIONS

5.1 Serious Rash, including Stevens-Johnson Syndrome

Serious rash requiring hospitalization and discontinuation of treatment has been reported in association with the use of modafinil. In pediatric clinical trials (modafinil is not approved in patients under 17 years for these indications), rash resulting in discontinuation occurred in approximately 0.8% of patients and included cases of possible Stevens-Johnson Syndrome (SJS) and multi-organ hypersensitivity. Rare cases of serious or life-threatening rash, including SJS, toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) have been reported in adults and children in worldwide postmarketing experience. Discontinue Vilafinil at the first sign of rash, unless the rash is clearly not drug-related. If rash occurs, do not restart unless another cause is identified.

5.2 Angioedema and Anaphylaxis

Angioedema and hypersensitivity (with rash, dysphagia, and bronchospasm) have been observed. Patients should be advised to discontinue therapy and immediately report any signs or symptoms suggesting angioedema or anaphylaxis (e.g., swelling of face, eyes, lips, tongue, or larynx; difficulty swallowing or breathing; hoarseness).

5.3 Multi-organ Hypersensitivity Reactions

Multi-organ hypersensitivity reactions, including at least one fatality in postmarketing experience, have occurred in close temporal association with the initiation of modafinil. Although there have been a limited number of reports, multi-organ hypersensitivity reactions may result in hospitalization or be life-threatening. Signs and symptoms were diverse; typically, although not exclusively, the patient presented with fever and rash associated with other organ system involvement. If multi-organ hypersensitivity is suspected, Vilafinil should be discontinued.

5.4 Persistent Sleepiness

Patients with abnormal levels of sleepiness who take Vilafinil should be advised that their level of wakefulness may not return to normal. Patients with excessive sleepiness, including those taking Vilafinil, should be frequently reassessed for their degree of sleepiness and, if appropriate, advised to avoid driving or any other potentially dangerous activity. Prescribers should also be aware that patients may not acknowledge sleepiness or drowsiness until directly asked about it during specific activities.

5.5 Psychiatric Symptoms

Psychiatric adverse experiences have been reported in patients treated with modafinil. Postmarketing adverse events associated with the use of modafinil have included mania, delusions, hallucinations, suicidal ideation, and aggression, some resulting in hospitalization. Many, but not all, patients had a prior psychiatric history. Caution should be exercised in administering Vilafinil to patients with a history of psychosis, depression, or mania. If psychiatric symptoms develop in association with Vilafinil administration, consider discontinuing the drug.

5.6 Effects on Ability to Drive and Use Machinery

Although Vilafinil has not been shown to produce functional impairment, any drug affecting the CNS may alter judgment, thinking, or motor skills. Patients should be cautioned about operating an automobile or other hazardous machinery until they are reasonably certain that Vilafinil therapy will not adversely affect their ability to engage in such activities.

5.7 Cardiovascular Events

In clinical studies, a greater proportion of patients on modafinil compared with placebo had a modest increase in heart rate and blood pressure. Increased monitoring of heart rate and blood pressure may be appropriate in patients on Vilafinil. Caution should be exercised when prescribing to patients with known cardiovascular disease. Vilafinil has not been evaluated in patients with a recent history of myocardial infarction or unstable angina.

5.8 Dependence and Misuse

Modafinil is a Schedule IV controlled substance in the United States. The potential for abuse and dependence exists. Carefully evaluate patients for a history of drug abuse and observe such patients closely, especially those with a history of stimulant or alcohol abuse.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

In pooled placebo-controlled trials in narcolepsy, OSA, and SWD, the most frequently reported adverse reactions (≥5%) that were more common with modafinil than placebo included:

Adverse Reaction	Modafinil (%)	Placebo (%)
Headache	34	23
Nausea	11	3
Nervousness	7	3

Rhinitis	7	6
Back pain	6	5
Diarrhea	6	5
Anxiety	5	1
Insomnia	5	1
Dizziness	5	4
Dyspepsia	5	4

Other reactions occurring more often than placebo included anorexia, dry mouth, pharyngitis, chest pain, hypertension, abnormal liver function tests, depression, palpitation, and tachycardia.

6.2 Postmarketing Experience

The following have been identified during post-approval use: serious skin reactions (SJS, TEN, DRESS), angioedema, anaphylaxis, multi-organ hypersensitivity, psychosis, mania, hallucinations, suicidal ideation, aggression, and agranulocytosis.

7 DRUG INTERACTIONS

Steroidal contraceptives: The effectiveness of steroidal contraceptives may be reduced when used with Vilafinil. Alternative or concomitant methods of contraception are recommended during treatment and for one month after discontinuation of Vilafinil.

CYP3A4 substrates (e.g., cyclosporine, midazolam, some calcium-channel blockers, some statins): Modafinil may decrease plasma concentrations of drugs metabolized by CYP3A4. Dose adjustment of the concomitant drug may be required.

CYP2C19 substrates (e.g., omeprazole, phenytoin, diazepam, propranolol): Modafinil may increase exposure to these drugs. Monitor and adjust doses as needed.

CYP2C9 substrates (e.g., warfarin): More frequent monitoring of prothrombin times/INR should be considered.

MAO inhibitors: Use caution; interaction data are limited.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There are no adequate and well-controlled studies of modafinil in pregnant women. Intrauterine growth restriction and spontaneous abortion have been reported in association with modafinil and armodafinil. Animal studies have shown developmental toxicity at clinically relevant exposures. Vilafinil should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. A pregnancy registry is available in some regions.

8.2 Lactation

It is not known whether modafinil or its metabolites are excreted in human milk. Caution should be exercised when Vilafinil is administered to a nursing woman.

8.3 Pediatric Use

Safety and effectiveness in patients below 17 years of age have not been established for the approved adult indications. Serious rash, including possible SJS, has been observed in pediatric clinical trials. Vilafinil is not approved for use in pediatric patients for these indications.

8.4 Geriatric Use

Clinical studies did not include sufficient numbers of patients aged 65 and over. In elderly patients, elimination of modafinil and its metabolites may be reduced as a consequence of aging. Consideration should be given to the use of lower doses.

8.5 Hepatic Impairment

In patients with severe hepatic impairment, the oral clearance of modafinil was decreased by about 60%, and the steady-state concentration was doubled compared with normal subjects. The dose should be reduced to one-half of that recommended for patients with normal hepatic function.

8.6 Renal Impairment

There is inadequate information to determine safety and efficacy in patients with severe renal impairment.

9 DRUG ABUSE AND DEPENDENCE

Modafinil is listed as a Schedule IV controlled substance in the United States. In humans, modafinil produces psychoactive and euphoric effects, alterations in mood, perception, thinking, and feelings typical of other CNS stimulants. Monitor patients for signs of misuse, abuse, or dependence.

10 OVERDOSAGE

Symptoms of overdose have included excitation or agitation, insomnia, and slight or moderate elevations in hemodynamic parameters. Other observed signs include restlessness, disorientation, confusion, hallucinations, nausea, diarrhea, tachycardia, bradycardia, hypertension, and chest pain. There is no specific antidote. Consider standard supportive measures. The effects of hemodialysis are unknown, but hemodialysis is unlikely to enhance elimination substantially given protein binding.

11 DESCRIPTION

Vilafinil contains modafinil, a wakefulness-promoting agent. Modafinil is a racemic compound. The chemical name is 2-[(diphenylmethyl)sulfinyl]acetamide.

Molecular formula: C15H15NO2S

Molecular weight: 273.35

Modafinil is a white to off-white, crystalline powder that is practically insoluble in water and sparingly soluble in methanol. Tablets typically contain inactive ingredients such as lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, povidone, magnesium stearate, and pregelatinized starch (exact composition varies by manufacturer).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanism(s) through which modafinil promotes wakefulness is unknown. Modafinil has wake-promoting actions similar to sympathomimetic agents including amphetamine and methylphenidate, although the pharmacologic profile is not identical. Modafinil-induced wakefulness can be attenuated by the α1-adrenergic receptor antagonist prazosin. Modafinil is not a direct- or indirect-acting dopamine receptor agonist. However, in vitro, modafinil binds to the dopamine transporter and inhibits dopamine reuptake. This activity has been associated in vivo with increased extracellular dopamine levels in some brain regions.

12.3 Pharmacokinetics

Modafinil is readily absorbed after oral administration, with peak plasma concentrations occurring at 2–4 hours. Food has no effect on overall bioavailability but may delay absorption by approximately one hour. Apparent steady state is reached after 2–4 days. Modafinil is moderately bound to plasma protein (approximately 60%), mainly to albumin. The major circulating metabolite is modafinil acid, which does not appear to contribute to the wake-promoting activity. Elimination half-life is approximately 15 hours. Excretion is primarily renal as metabolites. The R-enantiomer has a longer half-life than the S-enantiomer.

16 HOW SUPPLIED / STORAGE AND HANDLING

Vilafinil is typically supplied as 200 mg oral tablets in blister packs or bottles. Store at 20–25 °C (68–77 °F); excursions permitted to 15–30 °C (59–86 °F). Keep out of reach of children. Store securely because of the potential for misuse.

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling.

Instruct patients to stop Vilafinil and contact a physician at the first sign of rash, swelling, or allergic reaction.

Advise patients that Vilafinil is not a replacement for sleep and that they should continue good sleep hygiene and prescribed treatments (e.g., CPAP for OSA).

Counsel patients that steroidal contraceptives may be less effective and that additional or alternative contraception should be used during treatment and for one month after stopping.

Advise patients of possible psychiatric symptoms and to report mood changes, hallucinations, or suicidal thoughts.

Warn patients about the potential for impaired ability to drive or operate machinery if they remain sleepy.

PATIENT INFORMATION

VILAFINIL (vil-ah-FIN-il) • modafinil tablets

What is the most important information I should know about Vilafinil?

Vilafinil can cause serious side effects including a serious rash or a serious allergic reaction that may affect parts of the body such as the liver or blood cells. Stop taking Vilafinil and get medical help right away if you develop a rash, blistering, peeling skin, sores in the mouth, swelling of the face, eyes, lips, tongue, or throat, trouble swallowing or breathing, fever, yellowing of the skin or eyes, or unusual bruising.

Vilafinil is a federally controlled substance (C-IV) because it can be abused or lead to dependence. Keep it in a safe place.

What is Vilafinil?

Vilafinil contains modafinil, a prescription medicine used to improve wakefulness in adults who are very sleepy due to narcolepsy, obstructive sleep apnea, or shift work disorder. Vilafinil will not cure these conditions and will not take the place of getting enough sleep. If you have obstructive sleep apnea, continue using your CPAP machine or other prescribed treatments.

Who should not take Vilafinil?

Do not take Vilafinil if you are allergic to modafinil, armodafinil, or any of the ingredients in the tablet.

What should I tell my healthcare provider before taking Vilafinil?

Tell your healthcare provider if you:

- have heart problems, high blood pressure, or a history of heart attack or chest pain
- have or have had depression, psychosis, mania, or suicidal thoughts
- have liver or kidney problems
- have a history of drug or alcohol abuse
- are pregnant, plan to become pregnant, or are breastfeeding
- take hormonal birth control (pills, patches, rings, implants, or injections) — Vilafinil can make them less effective

Tell your healthcare provider about all medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I take Vilafinil?

- Take Vilafinil exactly as prescribed.
- For narcolepsy or sleep apnea, take it once a day in the morning.
- For shift work disorder, take it about 1 hour before your work shift starts.
- You may take it with or without food.
- Do not change your dose or stop taking it without talking to your healthcare provider.
- If you take too much, call your healthcare provider or poison control, or go to the nearest emergency room.

What should I avoid while taking Vilafinil?

- Do not drive or do other dangerous activities until you know how Vilafinil affects you. You may still be too sleepy to drive safely.
- Avoid drinking alcohol.
- Do not share Vilafinil with other people.

What are the possible side effects of Vilafinil?

Vilafinil may cause serious side effects including:

- Serious rash or allergic reaction (see above)
- Mental (psychiatric) problems, including depression, anxiety, hallucinations, mania, aggression, or suicidal thoughts
- Heart problems, including chest pain, fast heartbeat, or high blood pressure

The most common side effects are headache, nausea, nervousness, stuffy nose, diarrhea, back pain, anxiety, trouble sleeping, dizziness, and indigestion.

These are not all possible side effects. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Vilafinil?

- Store at room temperature between 68°F and 77°F (20°C and 25°C).
- Keep Vilafinil and all medicines out of the reach of children.
- Store in a secure place to prevent misuse.

General information

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use Vilafinil for a condition for which it was not prescribed. Do not give it to other people, even if they have the same symptoms you have. It may harm them and it is against the law to share a controlled substance.

END OF DOCUMENT

This comprehensive guide is intended for educational purposes only.
Always refer to the official prescribing information and consult a licensed healthcare professional.

Compiled in the style of a medication package insert • Based on publicly available FDA labeling for modafinil