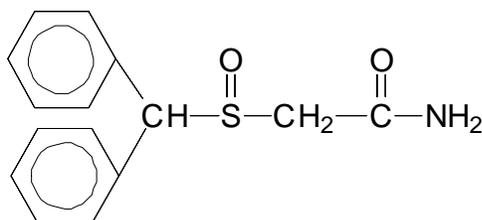


SPARLON™ (modafinil) Tablets [C-IV]**Rx Only****DESCRIPTION**

SPARLON (modafinil) is an orally administered agent for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD). Modafinil was initially developed and is also marketed as a wakefulness-promoting agent PROVIGIL® Tablets. Modafinil is a racemic compound. The chemical name for modafinil is 2-[(diphenylmethyl)sulfinyl]acetamide. The molecular formula is C₁₅H₁₅NO₂S and the molecular weight is 273.35.

The chemical structure is:



Modafinil is a white to off-white, crystalline powder that is very slightly soluble in water and practically insoluble in cyclohexane. It is sparingly soluble in methanol and slightly soluble in acetone. SPARLON tablets contain 85, 170, 255, 340, or 425 mg of modafinil and the following inactive ingredients: lactose, croscarmellose sodium, povidone, and magnesium stearate. The film coating for all tablet strengths contains: hypromellose, titanium dioxide, lactose, polyethylene glycol, and triacetin. In addition, the 170 mg and 340 mg tablets contain iron oxide yellow, and the 255 mg and 425 mg tablets contain FD&C Blue#2.

CLINICAL PHARMACOLOGY**Mechanism of Action and Pharmacology**

The precise mechanism(s) through which modafinil produces its therapeutic effects is unknown. Modafinil has attention promoting actions similar to sympathomimetic agents like amphetamine and methylphenidate, although the pharmacologic profile is not identical to that of sympathomimetic amines.

Modafinil is not a direct acting dopamine receptor agonist as evidenced by its lack of activity in several *in vivo* preclinical assays capable of measuring enhanced dopaminergic activity. *In vitro*,

modafinil binds to the dopamine reuptake site, causing an increase in extracellular dopamine, but does not increase dopamine release. In a preclinical model, the wakefulness induced by amphetamine, but not modafinil, is antagonized by the dopamine receptor antagonist haloperidol. The pattern of neuronal activation in the brain differs between modafinil and CNS stimulants such as methylphenidate and amphetamine.

Modafinil has weak to negligible interactions with receptors for norepinephrine, serotonin, dopamine, GABA, adenosine, histamine-3, melatonin, and benzodiazepines. Modafinil also does not inhibit the activities of MAO-B or phosphodiesterases II – V.

In humans, modafinil produces psychoactive and euphoric effects, alterations in mood, perception, thinking and feelings typical of other CNS stimulants. Modafinil is reinforcing, as evidenced by its self-administration in monkeys previously trained to self-administer cocaine; modafinil was also partially discriminated as stimulant-like.

The optical enantiomers of modafinil have similar pharmacological actions in animals. Two major metabolites of modafinil, modafinil acid and modafinil sulfone, do not appear to contribute to the CNS-activating properties of modafinil.

Pharmacokinetics

In adults, the pharmacokinetics of modafinil are proportional over the dose range of 200-600 mg/day; with an elimination half-life of approximately 15 hours. Dose proportionality is also evident in children and adolescents as suggested by population pharmacokinetic analysis. In children, modafinil half-life tends to be shorter than in adults. However, as children age through adolescence and into young adulthood, modafinil pharmacokinetics become more similar to that of adults.

Modafinil is a racemic compound, whose enantiomers have different pharmacokinetics (e.g., the half-life of the *R*-isomer is approximately three times that of the *S*-isomer in adult humans). The enantiomers do not interconvert. With repeated dosing in healthy adults, total exposure to the *R*-isomer is approximately three times that for the *S*-isomer.

Absorption

Modafinil is well absorbed after oral administration, with bioavailability of the tablet formulation being approximately equal to that of an aqueous suspension. Absolute bioavailability was not determined due to the aqueous insolubility (<1 mg/mL) of modafinil, which precluded intravenous administration. The t_{\max} in adults is, on average, approximately 2 to 4 hours. In children and adolescents, the t_{\max} is 2 to 3 hours. Data in healthy adults indicate that food affects the rate, but not the extent, of absorption.

Distribution

Modafinil is lipophilic in nature and is well distributed beyond the vascular system (V/F~0.9 L/kg) in adults. Modafinil is also well distributed in children, although it is important to note that body weight has a significant effect on V/F in children and adolescents, with volume of distribution increasing in a linear manner with weight. Modafinil is moderately protein bound (approximately 60%), mainly to albumin. Therefore, the potential for interactions with highly protein-bound drugs is minimal.

Metabolism

Modafinil is almost exclusively metabolized by the liver, with less than 10% of the administered dose excreted unchanged in the urine. Modafinil is primarily metabolized via a hydrolytic pathway and, to a lesser extent, via oxidative pathways. Metabolism occurs through hydrolytic deamidation, S-oxidation, aromatic ring hydroxylation, and glucuronide conjugation. In a clinical study conducted in healthy adults using radiolabeled modafinil, 81% of the administered dose was recovered over the 11-day study period, predominantly in the urine (80%) versus the feces (1%). Greater than 90% of the urinary radioactivity was excreted within 24 hours of administration. The major radioactive form that was recovered in urine was modafinil acid (40%), with at least 6 other metabolites present in lower concentrations. Alkalinization of the urine did not affect urinary excretion of modafinil or its primary circulating metabolites, modafinil acid and modafinil sulfone.

Following repeat-dose administration of modafinil, a time-dependent reduction in modafinil systemic exposure is observed in children/adolescents through autoinduction of CL/F. Plasma concentrations of one of modafinil's metabolites, modafinil sulfone, following multiple-dose administration of modafinil was often notably higher in children than that previously observed in

adults. In vitro data have shown that modafinil sulfone has the potential to induce CYP-mediated metabolism, including that of modafinil itself, which could contribute to the observed reduction in systemic exposure to modafinil following repeat-dose administration.

Elimination

The pharmacokinetic disposition of modafinil changes as children age through adolescence and into young adulthood. Children 6 to 7 years of age exhibit a half-life of approximately 7 hours with half-life approaching that of adults (half-life of 15 hours) as children age. Following repeat-dose administration of modafinil, a time-dependent reduction in systemic exposure as a result of change in clearance over time is observed in children/adolescents. Population pharmacokinetic modeling in children/adolescents indicates that the increase in clearance reaches a plateau by approximately week 6 of treatment (with an autoinduction half-life of about 12 days) and, as a result, measurements performed at week 9 are reflective of steady state.

Drug-Drug Interactions: Based on *in vitro* data, modafinil is metabolized partially by the 3A isoform subfamily of hepatic cytochrome P450 (CYP3A4). In addition, modafinil has the potential to inhibit CYP2C19 and induce CYP3A4, CYP2B6, and CYP1A2. Because modafinil and modafinil sulfone are reversible inhibitors of the drug-metabolizing enzyme CYP2C19, co-administration of modafinil with drugs such as diazepam, phenytoin and propranolol, which are largely eliminated via that pathway, may increase the circulating levels of those compounds. In addition, in individuals deficient in the enzyme CYP2D6 (i.e., 7-10% of the Caucasian population; similar or lower in other populations), the levels of CYP2D6 substrates such as tricyclic antidepressants and selective serotonin reuptake inhibitors, which have ancillary routes of elimination through CYP2C19, may be increased by co-administration of modafinil. Dose adjustments may be necessary for patients being treated with these and similar medications (See **PRECAUTIONS, Drug Interactions**).

Special Populations

The effect of gender, age, and weight on modafinil pharmacokinetics in children and adolescents with ADHD were examined using a population pharmacokinetic approach.

Gender Effect: The pharmacokinetics of modafinil are not affected by gender.

Age Effect: The estimated $t_{1/2}$ for the youngest patients (aged 6 to 7 years) studied is approximately 7 hours, and the $t_{1/2}$ for the oldest patients (aged 16 to 17 years) is approximately 10 hours. The general trend in the data indicates that there is a shift that begins between 9 and 11 years of age towards an increase in $t_{1/2}$.

Weight Effect: In children and adolescents, body weight has a significant effect on both clearance and volume of distribution of modafinil. Volume of distribution increases linearly with weight. Clearance also increases with increasing weight.

Based on these data, a modafinil dose of 340 mg in children and adolescents weighing less than 30 kg and 425 mg in children and adolescents weighing 30 kg or more consistently results in similar systemic exposures, indicating that the use of weight as a surrogate for dose selection is appropriate (See **DOSAGE and ADMINISTRATION**).

Race Effect: Modafinil pharmacokinetics are similar between Caucasian and African American populations. However, there were a limited number of patients in other race groups in the clinical trials which makes it difficult to fully elucidate any potential effect in these subgroups (approximately 90% of patients were Caucasian and African American).

Renal Impairment: In adults, severe chronic renal failure (creatinine clearance up to 20 mL/min) did not significantly affect the pharmacokinetics of modafinil administered at 200 mg, but exposure to modafinil acid was increased 9-fold (See **PRECAUTIONS**). No renal impairment studies have been conducted in children or adolescents.

Hepatic Impairment: Because modafinil is exclusively metabolized in the liver, hepatic impairment is expected to have an impact on the pharmacokinetic profile of the compound. Adult patients with cirrhosis have a decreased ability to metabolize modafinil, compared with healthy subjects. The oral clearance of modafinil was decreased by approximately 60%, and the steady-state concentration doubled, compared with values in healthy subjects. These results indicate that the dosage of modafinil should be reduced in patients with severe hepatic impairment (See **PRECAUTIONS and DOSAGE AND ADMINISTRATION**). No hepatic impairment studies have been specifically conducted in children or adolescents.

Pharmacodynamics

Clinical trial data indicate that administration of 340 mg of modafinil in children and adolescents with body weights less than 30 kg and 425 mg of modafinil in children and adolescents with body weights greater than or equal to 30 kg, achieve a sustained systemic exposure (approximately 150 µg·hr/mL) which correlates with a clinically significant effect. There were no observed trends towards a change in exposure or clinical effect with chronic dosing over 21 weeks.

CLINICAL TRIALS

The effectiveness of SPARLON in the treatment of ADHD was established in 3 randomized, double-blind, placebo-controlled studies of children and adolescents (ages 6 to 17) who met Diagnostic and Statistical Manual 4th edition (DSM-IV) criteria for ADHD (See **INDICATIONS and USAGE**).

Patients included in the phase 3 placebo-controlled studies were at least moderately ill according to the Clinical Global Impression of Severity (CGI-S) of ADHD symptoms. At baseline, 86% of the patients were moderately or markedly ill, and 14 % were severely ill. As measured by the Diagnostic Interview Schedule for Children, 4th edition (DISC-IV), 30% of the patients had the inattentive subtype, 5% had the hyperactive/impulsive subtype, while 65% of the patients had the combined subtype of ADHD. All baseline demographic characteristics were similar for patients in the SPARLON and placebo treatment groups. Of the 621 patients who received study drug, 71% were boys, and 76% of the patients were Caucasian. The mean age of the patients was 10.1 years (range 6 to 17 years); and most patients (67%) were less than 12 years of age. The mean weight was 41.4 kg (range 18.6 to 98.4 kg), with 68% of the patients weighing at least 30 kg.

In all studies, the primary assessment of efficacy was the total score from the teacher/physician-completed ADHD Rating Scale-IV (ADHD-RS-IV) (School Version). The primary outcome measure was the comparison of the mean change from baseline to endpoint for SPARLON- and placebo-treated patients. The ADHD RS-IV assesses the frequency of each of 18 individual criteria symptoms of ADHD in the DSM-IV on a 4-point Likert scale (0=never or rarely, 1=sometimes, 2=often or 3=very often). The ADHD-RS-IV (School Version) was completed by the investigator through interviewing the patient's weekday teacher.

In 2 identical, 9-week, randomized, double-blind, placebo-controlled, flexible-dosage studies of children and adolescents aged 6 to 17 (Study 1, N=200; Study 2, N=248), patients were randomized on a 2:1 basis to receive either SPARLON or placebo. SPARLON was administered as a single morning dose starting at 85 mg/day for 2 days, 170 mg/day for 5 days, and then increased at 85 mg increments weekly, according to clinical response and tolerability, up to a maximum of 425 mg. Statistically significant improvements in ADHD symptoms were observed in SPARLON-treated patients compared with placebo-treated patients as measured by ADHD-RS-IV (School Version) total score. See Table 1 for mean total scores at baseline and endpoint.

In Study 3, a 9-week, randomized, double-blind, placebo-controlled, fixed-dosage study of children and adolescents aged 6 to 17 (N=198), patients received either SPARLON (340 or 425 mg) or placebo. Patients weighing less than 30 kg received 340 mg of SPARLON and patients weighing at least 30 kg received 425 mg of SPARLON or matching placebo. Treatment was administered once daily, starting at 85 mg/day, and titrated at 85 mg increments every 2 days, to the fixed dose during the first 7 to 9 days. Statistically significant improvements in ADHD symptoms were observed in SPARLON-treated patients compared with placebo-treated patients as measured by ADHD-RS-IV (School Version) total score. See Table 1 for mean total scores at baseline and endpoint.

Table 1. ADHD Rating Scale-IV (School Version)

Mean (\pm SEM) ADHD Rating Scale-IV (School Version) Total Scores at Baseline and Endpoint for Studies 1, 2, and 3

	SPARLON		Placebo	
	Baseline Score	Endpoint Score	Baseline Score	Endpoint Score
Study 1	38.6	21.1	37.8	28.0
Study 2	35.7	20.7	35.3	28.0
Study 3	37.8	20.7	36.6	28.4

INDICATIONS AND USAGE

SPARLON is indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD).

The effectiveness of SPARLON in the treatment of ADHD was established in 3 randomized, double-blind, placebo-controlled studies in children and adolescents (age 6 – 17 years) who met DSM-IV criteria for ADHD (See **CLINICAL TRIALS**).

A diagnosis of ADHD (DSM-IV) implies the presence of hyperactive-impulsive or inattentive symptoms that cause impairment and that were present before age 7 years. The symptoms must be persistent, must be more severe than is typically observed in individuals at a comparable level of development, must cause clinically significant impairment, e.g., in social, academic, or occupational functioning, and must be present in 2 or more settings, e.g., school (or work) and at home. The symptoms must not be better accounted for by another mental disorder. For the Inattentive Type, at least 6 of the following symptoms must have persisted for at least 6 months: lack of attention to details/careless mistakes, lack of sustained attention, poor listener, failure to follow through on tasks, poor organization, avoids tasks requiring sustained mental effort, loses things, easily distracted, forgetful. For the Hyperactive-Impulsive Type, at least 6 of the following symptoms must have persisted for at least 6 months: fidgeting/squirming, leaving seat, inappropriate running/climbing, difficulty with quiet activities, “on the go”, excessive talking, blurting answers, can’t wait turn, intrusive. For a Combined Type diagnosis, both inattentive and hyperactive-impulsive criteria must be met.

Special Diagnostic Considerations

The specific etiology of ADHD is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but also of special psychological, educational, and social resources. Learning may or may not be impaired. The diagnosis must be based upon a complete history and evaluation of the patient and not solely on the presence of the required number of DSM-IV characteristics.

Need for Comprehensive Treatment Program

SPARLON is indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational, social) for patients with this syndrome. Drug treatment may not be indicated for all patients with this syndrome. Drug treatment is not

intended for use in the patient who exhibits symptoms secondary to environmental factors and/or other primary psychiatric disorders, including psychosis. Appropriate educational placement is essential in children and adolescents with this diagnosis and psychological intervention is often helpful. When remedial measures alone are insufficient, the decision to prescribe drug treatment medication will depend upon the physician's assessment of the chronicity and severity of the patient's symptoms.

Long-Term Use

The effectiveness of SPARLON for long-term use, i.e., for more than 9 weeks, has not been systematically evaluated in controlled trials. Therefore, the physician who elects to use SPARLON for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient (See **DOSAGE and ADMINISTRATION**).

CONTRAINDICATIONS

SPARLON is contraindicated in patients with known hypersensitivity to modafinil or its inactive ingredients.

WARNINGS

Psychiatric Symptoms

Psychiatric adverse experiences have been reported in children treated with SPARLON. In the short-term controlled clinical trials of SPARLON in children with ADHD, psychotic symptoms (described by the study physician as hallucinations) have been reported in 0.3% (2/664) of patients treated with SPARLON versus 0/308 of placebo-treated patients. Both events were generally short in duration (1 and 4 days), one event resolved without treatment change or discontinuation and the other resolved following treatment discontinuation. Neither of these two events required hospitalization. In the same trials, suicidal ideation (described by the study physician as suicidal statement, vague suicidal statement or suicide threat) was reported in 0.6% (4/664) of patients treated with SPARLON versus 0/308 of placebo-treated patients. All four events were generally short in duration (1 day), three events resolved without treatment change or discontinuation and one event resolved following treatment discontinuation. None of the events required hospitalization. Children treated with SPARLON should be monitored for clinical worsening, occurrence of suicidal ideation or changes in behavior.

Serious Rashes/Skin Reactions

In the short-term controlled clinical trials of SPARLON in children with ADHD, the overall incidence of rash reported in patients treated with SPARLON was 4% (29/664) versus 1% (4/308) in placebo-treated patients. In all clinical trials, among a total of 933 children diagnosed with ADHD and treated with SPARLON, 11 (1.1%) developed rashes or other possible skin/mucous membrane-associated reactions that resulted in hospitalizations and/or discontinuation from treatment. In no reported cases were skin reactions fatal. Two cases were consistent with a possible diagnosis of Stevens-Johnson Syndrome (SJS) that manifested as skin blistering and/or mucous membrane involvement (although 1 case was confounded by alternative infectious/drug etiologies). Neither of these patients was hospitalized. In both cases, the events resolved following discontinuation of study drug. No biopsy-confirmed cases of SJS were reported. Modafinil treatment should be discontinued in patients developing serious rash.

PRECAUTIONS

General

Patients should be aware that SPARLON contains the same active ingredient found in PROVIGIL, used to improve wakefulness in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder, and that SPARLON should not be used in combination with PROVIGIL or any other medications that contain modafinil.

Although modafinil 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 SPARLON therapy will not adversely affect their ability to engage in such activities.

Effects on Growth

As with other medications used to treat ADHD, growth should be monitored during treatment with SPARLON. In the phase 3 double-blind studies, there was a 0.9 cm increase in height in both the SPARLON- and placebo-treated patient groups. After 12 months of treatment in the phase 3 open-label study (n=533), there was a 4.1 cm increase in height with no change in the height percentile (51).

In the phase 3 double-blind studies, the SPARLON-treated patients lost on average 0.7 kg and placebo-treated patients gained on average 1.0 kg. In the phase 3 open-label study, patients treated with SPARLON gained an average of 1.9 kg while mean weight percentile decreased slightly from 62 to 57.

In the placebo-controlled studies, 36 (9%) patients receiving SPARLON and 3 (1%) patients receiving placebo, had a decrease of $\geq 7\%$ in body weight. For the majority of the patients, the magnitude of change in weight was relatively small compared with age and gender specific norms.

Patients Using Contraceptives

The effectiveness of steroidal contraceptives may be reduced when used with SPARLON tablets and for one month after discontinuation of therapy (See **Drug Interactions**). Alternative or concomitant methods of contraception are recommended for patients treated with SPARLON tablets, and for one month after discontinuation of SPARLON.

Cardiovascular System

In clinical studies of adults, signs and symptoms including chest pain, palpitations, dyspnea and transient ischemic T-wave changes on ECG were observed in three subjects in association with mitral valve prolapse or left ventricular hypertrophy. It is recommended that SPARLON tablets not be used in patients with a history of left ventricular hypertrophy or other underlying structural cardiac defects, or in patients with mitral valve prolapse who have experienced the mitral valve prolapse syndrome when previously receiving CNS stimulants. Such signs may include but are not limited to ischemic ECG changes, chest pain, or arrhythmia.

Central Nervous System

There have been reports of psychotic episodes associated with modafinil use. One healthy adult male volunteer developed ideas of reference, paranoid delusions, and auditory hallucinations in association with multiple daily 600 mg doses of modafinil and sleep deprivation. There was no evidence of psychosis 36 hours after drug discontinuation. Caution should be exercised when SPARLON is given to patients with a history of psychosis (See **WARNINGS, Psychiatric Symptoms**).

Patients with Severe Renal Impairment

In adult patients with severe renal impairment (mean creatinine clearance = 16.6 mL/min), a 200 mg single dose of modafinil did not lead to increased exposure to modafinil but resulted in much higher exposure to the inactive metabolite, modafinil acid, than is seen in subjects with normal renal function. There is little information available about the safety of such levels of this metabolite (See **CLINICAL PHARMACOLOGY**).

Patients with Severe Hepatic Impairment

In adult patients with severe hepatic impairment, with or without cirrhosis (See **CLINICAL PHARMACOLOGY**), SPARLON should be administered at a reduced dose as the clearance of modafinil was decreased compared to that in normal subjects (See **DOSAGE and ADMINISTRATION**).

Information for Patients

Patients, parents or caregivers should be informed of the availability of a patient information leaflet, and they should be instructed to read the leaflet prior to taking SPARLON. See Patient Information at the end of this labeling for the text of the leaflet provided for patients.

Pregnancy

Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Patients should be cautioned regarding the potential increased risk of pregnancy when using steroidal contraceptives (including depot or implantable contraceptives) with SPARLON and for one month after discontinuation of therapy (See *Impairment of Fertility and Pregnancy*).

Nursing

Patients should be advised to notify their physician if they are breast feeding an infant.

Concomitant Medication

Patients should be advised to inform their physician if they are taking, or plan to take, any prescription or over-the-counter drugs, because of the potential for interactions between SPARLON and other drugs.

Alcohol

Patients should be advised that the use of SPARLON in combination with alcohol has not been studied. Patients should be advised that it is prudent to avoid alcohol while taking SPARLON.

Allergic Reactions

Patients should be advised to notify their physician if they develop a rash, hives, or a related allergic phenomenon.

Drug Interactions

CNS Active Drugs

Methylphenidate - In a single-dose study in healthy adult volunteers, simultaneous administration of modafinil (200 mg) with methylphenidate (40 mg) did not cause any significant alterations in the pharmacokinetics of either drug. However, the absorption of modafinil may be delayed by approximately one hour when coadministered with methylphenidate.

Dextroamphetamine - In a single dose study in healthy adult volunteers, simultaneous administration of modafinil (200 mg) with dextroamphetamine (10 mg) did not cause any significant alterations in the pharmacokinetics of either drug. However, the absorption of modafinil may be delayed by approximately one hour when coadministered with dextroamphetamine.

Clomipramine - The coadministration of a single dose of clomipramine (50 mg) on the first of three days of treatment with modafinil (200 mg/day) in healthy adult volunteers did not show an effect on the pharmacokinetics of either drug. However, one incident of increased levels of clomipramine and its active metabolite desmethylclomipramine has been reported in a patient with narcolepsy during treatment with modafinil.

Triazolam – In the drug interaction study between modafinil and ethinyl estradiol (EE₂), on the same days as those for the plasma sampling for EE₂ pharmacokinetics, a single dose of triazolam (0.125 mg) was also administered. Mean C_{max} and AUC_{0-∞} of triazolam were decreased by 42% and 59%, respectively, and its elimination half-life was decreased by approximately an hour after the modafinil treatment.

Monoamine Oxidase (MAO) Inhibitors - Interaction studies with monoamine oxidase inhibitors have not been performed. Therefore, caution should be used when concomitantly administering MAO inhibitors and modafinil.

Other Drugs

Warfarin - There were no significant changes in the pharmacokinetic profiles of R- and S-warfarin in healthy adult subjects given a single dose of racemic warfarin (5 mg) following chronic administration of modafinil (200 mg/day for 7 days followed by 400 mg/day for 27 days) relative to the profiles in subjects given placebo. However, more frequent monitoring of prothrombin times/INR is advisable whenever SPARLON is coadministered with warfarin (See **CLINICAL PHARMACOLOGY, Pharmacokinetics**, Drug-Drug Interactions).

Ethinyl Estradiol - Administration of modafinil to female adult volunteers once daily at 200 mg/day for 7 days followed by 400 mg/day for 21 days resulted in a mean 11% decrease in C_{max} and 18% decrease in AUC_{0-24} of ethinyl estradiol (EE_2 ; 0.035 mg; administered orally with norgestimate). There was no apparent change in the elimination rate of ethinyl estradiol.

Cyclosporine - One case of an interaction between modafinil and cyclosporine, a substrate of CYP3A4, has been reported in a 41 year old woman who had undergone an organ transplant. After one month of administration of 200 mg/day of modafinil, cyclosporine blood levels were decreased by 50%. The interaction was postulated to be due to the increased metabolism of cyclosporine, since no other factor expected to affect the disposition of the drug had changed. Dosage adjustment for cyclosporine may be needed.

Potential Interactions with Drugs That Inhibit, Induce, or are Metabolized by Cytochrome P-450 Isoenzymes and Other Hepatic Enzymes

In *in vitro* studies using primary human hepatocyte cultures, modafinil and modafinil sulfone were shown to induce CYP1A2, CYP2B6 and CYP3A4 in a concentration-dependent manner. In pediatric patients, concentrations of the modafinil sulfone metabolite are high and sustained. Induction may be more prominent in children due to their higher exposure to modafinil sulfone. Therefore, caution needs to be exercised when SPARLON is coadministered with drugs that depend on these three enzymes for their clearance (e.g., theophylline). Specifically, lower blood levels of such drugs could result (See *Other Drugs*, Cyclosporine above).

The exposure of human hepatocytes to modafinil *in vitro* produced an apparent concentration-related suppression of expression of CYP2C9 activity suggesting that there is a potential for a metabolic interaction between modafinil and the substrates of this enzyme (e.g., S-warfarin and

phenytoin). However, a suppressive effect on CYP2C9 activity was not reproduced in a subsequent *in vitro* study, and in a clinical study in healthy adult volunteers, chronic modafinil treatment did not show a significant effect on the single-dose pharmacokinetics of warfarin when compared to placebo (See **PRECAUTIONS, Drug Interactions, Warfarin**).

In vitro studies using human liver microsomes showed that modafinil reversibly inhibited CYP2C19 at pharmacologically relevant concentrations of modafinil. CYP2C19 is also reversibly inhibited, with slightly higher potency, by a circulating metabolite, modafinil sulfone. In adults, sustained exposure to modafinil sulfone is observed, but at concentrations that are lower than those of the parent compound. In pediatric patients, concentrations of the sulfone metabolite are often higher than modafinil, suggesting that a significant inhibitory effect on CYP2C19 activity may occur (See **CLINICAL PHARMACOLOGY, Pharmacokinetics, Metabolism**). Drugs that are largely eliminated via CYP2C19 metabolism, such as diazepam, propranolol, phenytoin, omeprazole or S-mephenytoin may have prolonged elimination upon coadministration with SPARLON and may require dosage reduction and monitoring for toxicity.

Tricyclic antidepressants - CYP2C19 also provides an ancillary pathway for the metabolism of certain tricyclic antidepressants (e.g., clomipramine, atomoxetine and desipramine) that are primarily metabolized by CYP2D6. In tricyclic-treated patients deficient in CYP2D6 (i.e., those who are poor metabolizers of debrisoquine; 7-10% of the Caucasian population; similar or lower in other populations), the fraction of metabolic elimination that proceeds via CYP2C19 may be substantially increased. SPARLON may cause elevation of the levels of the tricyclics in this subset of patients. Physicians should be aware that a reduction in the dose of tricyclic agents might be needed in these patients.

In addition, due to the partial involvement of CYP3A4 in the metabolic elimination of modafinil, coadministration of potent inducers of CYP3A4 (e.g., carbamazepine, phenobarbital, rifampin) or inhibitors of CYP3A4 (e.g., ketoconazole, itraconazole) could alter the plasma levels of modafinil.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Carcinogenicity studies were conducted in which modafinil was administered in the diet to mice for 78 weeks and to rats for 104 weeks at doses of 6, 30 and 60 mg/kg/day. The highest dose studied is 0.5 times (mouse) or the same as (rat) the maximum recommended human daily dose of 425 mg on a mg/m² basis. There was no evidence of tumorigenesis associated with modafinil administration in these studies, but because the mouse study used an inadequate high dose that was not representative of a maximum tolerated dose, the carcinogenic potential of modafinil has not been fully evaluated.

Mutagenesis

There was no evidence of mutagenic or clastogenic potential of modafinil in a series of assays. It was not mutagenic in the *in vitro* Ames bacterial reverse mutation test, the *in vitro* mouse lymphoma/TK locus assay in the presence or absence of metabolic activation; and it was not clastogenic in the *in vitro* human lymphocyte chromosomal aberration assay in the presence or absence of metabolic activation, or in two *in vivo* mouse bone marrow micronucleus assays. Modafinil did not increase unscheduled DNA synthesis in rat hepatocytes. In a cell transformation assay in BALB/3T3 mouse embryo cells, modafinil did not cause an increase in the frequency of transformed foci in the presence or absence of metabolic activation.

Impairment of Fertility

Oral administration of modafinil to male and female rats had no effects on fertility when administered prior to and throughout mating, and continued in females through day 7 of gestation, at doses up to 480 mg/kg/day (9 times the maximum recommended human daily dose of 425 mg/day on a mg/m² basis).

Pregnancy

Pregnancy Category C: Modafinil administered orally to pregnant rats throughout the period of organogenesis caused, in the absence of maternal toxicity, an increase in resorptions and an increased incidence of hydronephrosis and skeletal variations in the offspring at a dose of 200 mg/kg/day (4 times the maximum recommended human daily dose of 425 mg/day on a mg/m² basis) but not at 100 mg/kg/day. However, in a subsequent study of up to 480 mg/kg/day (9

times the maximum recommended human daily dose on a mg/m^2 basis), which included maternally toxic doses, no adverse effects on embryofetal development were seen.

Modafinil administered orally to pregnant rabbits throughout the period of organogenesis at doses up to 100 $\text{mg}/\text{kg}/\text{day}$ (4 times the maximum recommended human daily dose on a mg/m^2 basis) had no effects on embryofetal development.

However, in a subsequent study in pregnant rabbits, increased resorptions, and increased alterations in fetuses from a single litter (open eye lids, fused digits, rotated limbs), were observed at 180 $\text{mg}/\text{kg}/\text{day}$ (7 times the maximum recommended human daily dose on a mg/m^2 basis), a dose that was also maternally toxic.

Modafinil administered orally to rats throughout gestation and lactation at doses up to 200 $\text{mg}/\text{kg}/\text{day}$ (4 times the maximum recommended human daily dose on a mg/m^2 basis), had no effects on the postnatal development of the offspring.

There are no adequate and well-controlled studies in pregnant women. Modafinil should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery

The effect of modafinil on labor and delivery in humans has not been systematically investigated. Seven normal births occurred in patients who had received modafinil during pregnancy. One patient gave birth 3 weeks earlier than the expected range of delivery dates (estimated using ultrasound) to a healthy male infant. One woman with a history of spontaneous abortions suffered a spontaneous abortion while being treated with modafinil.

Nursing Mothers

It is not known whether modafinil or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when SPARLON tablets are administered to a nursing woman.

Pediatric Use

Safety and effectiveness of SPARLON in individuals below 6 years of age have not been established.

A 13-week study was conducted in young rats to evaluate the effects of SPARLON on skeletal growth, sexual development and neurobehavioral development. Rat pups were treated with 30, 120 or 240 mg/kg/day (0.5 to 4 times the maximum human daily dose of 425 mg on a mg/m² basis) of modafinil via oral gavage beginning on Day 10 *post partum* and continuing through adulthood. No effect on skeletal growth as assessed by femur length measurements was observed at completion of the dosing period. Sexual maturation (vaginal patency, preputial separation, estrus cycling, sperm counts, and mating performance) were not affected. A slight decrease in motor activity was noted on Days 23 (≥ 30 mg/kg/day) and Days 96-99 (≥ 120 mg/kg/day) *post partum*; this was not seen after a 4 week recovery period. There were no effects on learning and memory tests. The significance of these findings to humans is unknown.

Geriatric Use

Safety and effectiveness in individuals above 65 years of age have not been established.

ADVERSE REACTIONS

Modafinil was administered to 933 children or adolescent patients with ADHD in clinical studies. In these clinical studies, the majority of adverse events (90%) were reported to be mild to moderate.

The most commonly observed adverse events ($\geq 5\%$) associated with the use of SPARLON more frequently than placebo-treated patients in the placebo-controlled clinical studies were insomnia, headache, anorexia (decreased appetite), abdominal pain, fever, and nervousness. The adverse event profile was similar across these studies.

In the phase 3, placebo-controlled clinical trials, 5% (21 of 420) of the patients who received SPARLON discontinued due to an adverse experience compared to 3% (7 of 213) of patients who received placebo. The most frequent reasons for discontinuation were insomnia (1%, n=5), abdominal pain (<1%, n=3), and emotional lability (<1%, n=3).

Incidence in Controlled Trials

The following table presents the adverse experiences that occurred at a rate of 2% or more and were more frequent in patients treated with SPARLON than in placebo patients in the principal, placebo-controlled clinical trials.

The prescriber should be aware that the figures provided below cannot be used to predict the frequency of adverse experiences in the course of usual medical practice, where patient characteristics and other factors may differ from those occurring during clinical studies. Similarly, the cited frequencies cannot be directly compared with figures obtained from other clinical investigations involving different treatments, uses, or investigators. Review of these frequencies, however, provides prescribers with a basis to estimate the relative contribution of drug and non-drug factors to the incidence of adverse events in the population studied.

Table 2. Incidence of Treatment-Emergent Adverse Experiences In Parallel-Group, Placebo-Controlled Clinical Trials with SPARLON¹

Body System	Preferred Term	Modafinil (n = 420)	Placebo (n = 213)
Body as a Whole	Headache	20%	13%
	Abdominal Pain	10%	8%
	Fever	5%	3%
	Pain	3%	2%
Digestive	Anorexia	16%	3%
	Nausea	4%	2%
	Dry Mouth	2%	1%
	Dyspepsia	2%	1%
	Gastroenteritis	2%	1%
Hemic/Lymphatic	Ecchymosis	2%	0%
Metabolic/Nutritional	Weight Loss	4%	1%
Nervous	Insomnia	27%	4%
	Nervousness	5%	4%
	Dizziness	2%	1%
Skin/Appendages	Rash	4%	2%

¹ Events reported in the three double-blind placebo controlled clinical studies by at least 2% of patients treated with SPARLON that were more frequent than in the placebo group are included; incidence is rounded to the nearest 1%. The adverse experience terminology is coded using a standard modified COSTART Dictionary.

Events for which the SPARLON incidence was 1%, but greater than placebo are not listed in the table. These events include: twitching, depression, tremor, and pruritus.

Events for which the SPARLON incidence was at least 1%, but equal to or less than placebo are not listed in the table. These events included the following: infection, accidental injury, flu syndrome, bacterial infection, allergic reaction, viral infection, tachycardia, vomiting, diarrhea, emotional lability, somnolence, agitation, anxiety, hostility, increased cough, rhinitis, pharyngitis, sinusitis,

Vital Sign Changes

In the Phase 3 studies, there were no differences between the SPARLON and placebo treatment groups with respect to changes in vital signs; including heart rate, systolic and diastolic blood pressure, and body temperature.

Weight Changes

In the phase 3 double-blind studies, the SPARLON-treated patients had on average a 0.7 kg decrease in weight and placebo-treated patients had on average a 1.0 kg increase. After 12 months of treatment in the phase 3 open-label study, patients treated with SPARLON had on average an increase of 1.9 kg while mean weight percentile decreased slightly from 62 to 57 (See **PRECAUTIONS**).

Laboratory Changes

Hematology

In phase 3, placebo-controlled studies, there were no marked differences between the SPARLON and placebo treatment groups in the incidence of clinically significantly abnormal hematology values. Low ANC values ($\leq 1 \times 10^9/L$) were seen in 2% patients in both the SPARLON treatment group and in the placebo treatment group. Low WBC values ($\leq 3 \times 10^9/L$) were seen in 2% of the SPARLON-treated patients and in 1% placebo-treated patients. The majority of the patients with clinically significantly abnormal ANC and/or WBC values also had corresponding elevations in the lymphocytes and/or monocytes, suggesting the presence of a viral syndrome in these patients.

Blood Chemistry

In the phase 3 placebo-controlled studies, the only notable differences between the SPARLON and placebo treatment groups were a mean decrease in uric acid (19.4 $\mu\text{mol/L}$) and mean increases in alkaline phosphatase (16.8 units/L) and GGT (6.3 units/L). Even with these changes, most values remained within normal range. The effect of SPARLON on alkaline phosphatase and GGT appear to be more pronounced in the higher dosage groups (340 and 425 mg/day), and were not accompanied by increases in ALT, AST, or total bilirubin. Elevations of alkaline phosphatase and GGT have previously been observed in adults.

ECG Changes

In the phase 3, placebo-controlled studies, there were no differences between the SPARLON and placebo treatment groups with respect to ECG interval durations, including QTc.

Postmarketing Reports

The following adverse reactions have been identified during post-approval use of modafinil. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Decisions to include these reactions in labeling are typically based on one or more of the following factors: (1) seriousness of the reaction, (2) frequency of the reporting, or (3) strength of causal connection to modafinil.

Central Nervous System: symptoms of psychosis, symptoms of mania

Dermatologic: rare reports of serious skin reactions (including suspected cases of both erythema multiforme and Stevens-Johnson syndrome)

Hematologic: agranulocytosis

Hypersensitivity: urticaria (hives), angioedema

DRUG ABUSE AND DEPENDENCE

Controlled Substance Class

Modafinil (SPARLON) is listed in Schedule IV of the Controlled Substances Act.

Abuse Potential and Dependence

In addition to its wakefulness-promoting effect and increased locomotor activity in animals, in humans, modafinil produces psychoactive and euphoric effects, alterations in mood, perception, thinking and feelings typical of other CNS stimulants. In *in vitro* binding studies, modafinil binds to the dopamine reuptake site and causes an increase in extracellular dopamine, but no increase in dopamine release. Modafinil is reinforcing, as evidenced by its self-administration in monkeys previously trained to self-administer cocaine. In some studies, modafinil was also partially discriminated as stimulant-like. Physicians should follow patients closely, especially those with a history of drug and/or stimulant (e.g., methylphenidate, amphetamine, or cocaine) abuse. Patients should be observed for signs of misuse or abuse (e.g., incrementation of doses or drug-seeking behavior).

The abuse potential of modafinil (200, 400, and 800 mg) was assessed relative to methylphenidate (45 and 90 mg) in an inpatient study in individuals experienced with drugs of abuse. Results from this clinical study demonstrated that modafinil produced psychoactive and euphoric effects and feelings consistent with other scheduled CNS stimulants (methylphenidate).

Withdrawal

The abrupt withdrawal from SPARLON treatment did not have any effect on physical or emotional health of the patients as assessed by the STESS (Subject's Treatment Emergent Symptom Scale). In addition, there was no evidence of symptom rebound or adverse events suggesting a drug-discontinuation or withdrawal syndrome.

OVERDOSAGE

Human Experience

In clinical trials, a total of 151 protocol-specified doses ranging from 1000 to 1600 mg/day (more than 2 times the recommended daily dose of 425 mg) have been administered to 32 subjects, including 13 subjects who received doses of 1000 or 1200 mg/day for 7 to 21 consecutive days. In addition, several intentional acute overdoses occurred; the two largest being 4500 mg and 4000 mg taken by two subjects participating in foreign depression studies. None of these study subjects experienced any unexpected or life-threatening effects. Adverse experiences that were reported at these doses included excitation or agitation, insomnia, and slight or moderate elevations in hemodynamic parameters. Other observed high-dose effects in clinical studies have included anxiety, irritability, aggressiveness, confusion, nervousness, tremor, palpitations, sleep disturbances, nausea, diarrhea and decreased prothrombin time.

From post-marketing experience, there have been no reports of fatal overdoses involving modafinil alone (doses up to 12 grams). Overdoses involving multiple drugs, including modafinil, have resulted in fatal outcomes. Symptoms most often accompanying modafinil overdose, alone or in combination with other drugs have included: insomnia; central nervous system symptoms such as restlessness, disorientation, confusion, excitation and hallucination; digestive changes such as nausea and diarrhea; and cardiovascular changes such as tachycardia, bradycardia, hypertension and chest pain.

Cases of accidental ingestion/overdose have been reported in children as young as 11 months of age. The highest reported accidental ingestion on a mg/kg basis occurred in a three-year-old boy who ingested 800-1000 mg (50-63 mg/kg) of modafinil. The child remained stable. The symptoms associated with overdose in children were similar to those observed in adults.

Overdose Management

No specific antidote to the toxic effects of modafinil overdose has been identified to date. Such overdoses should be managed with primarily supportive care, including cardiovascular monitoring. If there are no contraindications, induced emesis or gastric lavage should be considered. There are no data to suggest the utility of dialysis or urinary acidification or alkalization in enhancing drug elimination. The physician should consider contacting a poison-control center on the treatment of any overdose.

DOSAGE and ADMINISTRATION

Initial Treatment

SPARLON should be taken as a single dose, in the morning, with or without food. Dosage should be individualized according to the needs and responses of the patient. In clinical trials, treatment was initiated at 85 mg /day. The daily dosage was increased by 85 mg increments every 2 to 7 days until the optimum or target daily dose was achieved. Doses above 425 mg have not been systematically evaluated. (See **CLINICAL TRIALS**).

The following target daily doses of SPARLON are recommended:

Patients less than 30 kg of body weight: 340 mg

Patients at least 30 kg of body weight: 425 mg

Maintenance/Extended Treatment

There is no evidence available from controlled trials to indicate how long the patient with ADHD should be treated with SPARLON. It is generally agreed, however, that pharmacological treatment of ADHD may be needed for extended periods. Nevertheless, the physician who elects to use SPARLON for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient.

Dosage adjustment should be considered for concomitant medications that are substrates for CYP3A4, such as triazolam and cyclosporine (See **PRECAUTIONS, Drug Interactions**).

Drugs that are largely eliminated via CYP2C19 metabolism, such as diazepam, propranolol, phenytoin (also via CYP2C9) or S-mephenytoin may have prolonged elimination upon coadministration with SPARLON and may require dosage reduction and monitoring for toxicity.

In patients with severe hepatic impairment, the dose of SPARLON should be reduced to one-half of that recommended for patients with normal hepatic function (See **CLINICAL PHARMACOLOGY** and **PRECAUTIONS**).

There is inadequate information to determine safety and efficacy of dosing in patients with severe renal impairment (See **CLINICAL PHARMACOLOGY** and **PRECAUTIONS**).

HOW SUPPLIED:

SPARLON (modafinil) Tablets

- | | |
|---------------|---|
| 85 mg | Each capsule-shaped, white, film-coated tablet is debossed with the Cephalon "C" logo on one side and "111" on the other.
NDC 63459-111-60 - Bottles of 60
NDC 63459-111-01 - Bottles of 100 |
| 170 mg | Each capsule-shaped, light yellow, film-coated tablet is debossed with the Cephalon "C" logo on one side and "112" on the other.
NDC 63459-112-60 - Bottles of 60
NDC 63459-112-01 - Bottles of 100 |
| 255 mg | Each capsule-shaped, light blue, film-coated tablet is debossed with the Cephalon "C" logo on one side and "113" on the other.
NDC 63459-113-30 - Bottles of 30
NDC 63459-113-01 - Bottles of 100 |
| 340 mg | Each capsule-shaped, dark yellow, film-coated tablet is debossed with the Cephalon "C" logo on one side and "114" on the other.
NDC 63459-114-30 - Bottles of 30
NDC 63459-114-01 - Bottles of 100 |
| 425 mg | Each capsule-shaped, dark blue, film-coated tablet is debossed with the Cephalon "C" logo on one side and "115" on the other.
NDC 63459-115-30 - Bottles of 30
NDC 63459-115-01 - Bottles of 100 |

Store at 20° - 25° C (68° - 77° F).

Manufactured for:

Cephalon, Inc.
Frazer, PA 19355

U.S. Patent Nos. RE37,516 / 6,346,548

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November 2005
SPAR-xxx

INFORMATION FOR PATIENTS OR THEIR PARENTS OR CAREGIVERS
SPARLON Tablets [C-IV]
Generic name: modafinil

Read the Patient Information that comes with SPARLON before you start taking it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your doctor about your condition or treatment.

What is SPARLON?

SPARLON is a medicine to treat Attention-Deficit/Hyperactivity Disorder (ADHD). SPARLON contains modafinil. Your doctor has prescribed this medicine as part of an overall treatment plan to control your symptoms of ADHD.

SPARLON is a controlled substance [C-IV]. This means that SPARLON may be a target for people who abuse medicines or street drugs. Keep your SPARLON in a safe place. Giving away SPARLON is against the law.

What is ADHD?

ADHD has 3 main types of symptoms: inattention, hyperactivity, and impulsiveness. Symptoms of inattention include not paying attention, making careless mistakes, not listening, not finishing tasks, not following directions, and being easily distracted. Symptoms of hyperactivity and impulsiveness include fidgeting, talking excessively, running around at inappropriate times, and interrupting others. Some patients have more symptoms of hyperactivity and impulsiveness while others have more symptoms of inattentiveness. Some patients have all 3 types of symptoms.

Many people have symptoms like these from time to time, but patients with ADHD have these symptoms more than others their age. Symptoms must be present for at least 6 months to be certain of the diagnosis.

Who should NOT take SPARLON?

Do not take SPARLON if you are allergic to any of its ingredients. The active ingredient is modafinil. See the end of this leaflet for a complete list of ingredients.

Do not take SPARLON if you are already taking PROVIGIL[®] Tablets, or any other medicines that contain modafinil.

Before starting SPARLON tell your doctor

- about all your medical conditions, including if you:
 - are pregnant, are planning to become pregnant, or are breastfeeding. It is not known if SPARLON may harm your unborn baby, or if SPARLON passes into your milk and if it can harm your baby.
 - have high blood pressure or heart problems.
 - have liver or kidney problems.
 - have abused medicines called “stimulants” or street drugs.
 - have or had a mental problem called psychosis.

- about all medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. SPARLON and many other medicines can interact with each other causing side effects. SPARLON may affect the way other medicines work, and other medicines may affect how SPARLON works. Keep a list of all medicines you take. Your doctor or pharmacist will tell you if it is safe to take SPARLON and other medicines together. Do not take other medicines with SPARLON unless your doctor has told you it is okay.

SPARLON can affect hormonal birth control methods (contraceptives). Women who use hormonal contraceptives such as birth control pills, shots, implants, intrauterine devices (IUDs) or patches, may have a higher chance for getting pregnant while taking SPARLON, and for one month after stopping SPARLON. Talk to your doctor about birth control methods that are right for you while using SPARLON.

How should I take SPARLON?

- Take SPARLON exactly as prescribed by your doctor. Your doctor will prescribe the dose of SPARLON that is right for you. Do not change your dose of SPARLON without talking to your doctor. Do not take more SPARLON than prescribed.
- You can take SPARLON with or without food.
- You should take SPARLON once each day in the morning.
- If you take more than your prescribed dose, or take SPARLON too late in the day, you may find it harder to go to sleep. Call your doctor if you have any concerns.

Take the dose prescribed by your doctor. Your doctor may adjust the amount of drug you take until it is right for you. From time to time, your doctor may interrupt your treatment to check your symptoms while you are not taking the drug.

What should I avoid while taking SPARLON?

- Do not take other medicines including prescription and non-prescription medicines, vitamins or herbal supplements unless your doctor has told you it is okay.
- You should avoid drinking alcohol.

What are the possible side effects of SPARLON?

The most common side effects of SPARLON are insomnia, headache, decreased appetite, abdominal pain, fever, and nervousness.

SPARLON may cause the following infrequent serious side effects. Call your doctor or get emergency help if you have any of these or any other serious side effects while taking SPARLON:

- mental problems
- allergic reactions, such as a rash, hives or other allergic reaction

Some effects of SPARLON on the brain are similar to other medications called “stimulants”. If you have a history of drug and/or stimulant use or abuse you should discuss this with your doctor before starting SPARLON.

Tell your doctor if you get any side effects while taking SPARLON.

These are not all the side effects of SPARLON. For more information, ask your doctor or pharmacist.

How should I store SPARLON?

- Store SPARLON at room temperature, 68° to 77° F (20° to 25° C).
- Store SPARLON in a safe place.
- Keep SPARLON and all medicines out of the reach of children.

General information about SPARLON

Medicines are sometimes prescribed for conditions that are not listed in patient information leaflets. Do not use SPARLON for a condition for which it is not prescribed. This medication is for your use only. Do not share this medication with others.

This leaflet summarizes the most important information about SPARLON. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about SPARLON that is written for health professionals. For more information, please call 1-800-896-5855, or go to www.SPARLON.com.

What are the ingredients in SPARLON?

Active Ingredient: modafinil

Inactive Ingredients: lactose, croscarmellose sodium, povidone, and magnesium stearate. The coating on the outside of the tablet contains: hypromellose, titanium dioxide, lactose, polyethylene glycol, and triacetin. Some tablet coatings also contain: iron oxide yellow or FD&C Blue #2.

Rx Only

Month 200X

Cephalon, Inc. Frazer, PA 19355

This Patient Information Leaflet has been approved by the U.S. Food and Drug Administration
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