PRODUCT MONOGRAPH

[N] pms-NABILONE

Nabilone

Capsules: 0.25 mg, 0.5 mg, 1 mg

Professed Standard

Antiemetic

PHARMASCIENCE INC.
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H4P 2T4

Date of Preparation:
February 29, 2012

Submission Control No.: 138763

[N] pms-NABILONE

Nabilone Capsules

THERAPEUTIC CLASSIFICATION

Antiemetic Agent

ACTION

pms-NABILONE (nabilone) is a synthetic cannabinoid with antiemetic properties which have been found to be of value in the management of some patients with nausea and vomiting associated with cancer chemotherapy. It also has sedative and psychotropic effects.

After oral administration, comparable peak plasma levels of nabilone and of its carbinol metabolite were attained within 2 hours. The combined plasma concentrations of nabilone and of its carbinol metabolite accounted for, at most, 10 to 20% of the total radiocarbon concentration in plasma. The plasma half-life of nabilone was approximately 2 hours, while that of the total radiocarbon was of the order of 35 hours.

Of the two major possible metabolic pathways, stereo-specific enzymatic reduction and direct enzymatic oxidation, the latter appears to be the more important in man.

The drug and its metabolites are eliminated mainly in the feces (approximately 65%) and to a lesser extent in the urine (approximately 20%). The major excretory pathway is the bilary system.

Comparative Bioavailability Studies
A single dose 2-way cross-over comparative bioavailability study of pms-NABILONE 1 mg Capsules (nabilone, Pharmascience Inc.), was performed versus CESAMET (nabilone) 1 mg Capsules (Valeant Canada Ltd.) administered as 1 x 1 mg dose to healthy male volunteers in the fasting state (n=18). The results are summarized in the following table:

SUMMARY TABLE OF THE COMPARATIVE BIOAVAILABILITY DATA

Nabilone (1 x 1 mg capsule) From measured data **uncorrected for potency** Geometric Mean Arithmetic Mean (CV %)				
Parameter	Test*	Reference†	% Ratio of Geometric Means	90% Confidence Interval
AUC_T (pg·h/mL)	3163.1 3226.6 (29.4)	2868.1 2956.4 (26.3)	110.29	101.85-119.42
AUC_I (pg·h/mL)	3290.7 3352.7 (28.5)	2970.1 3057.5 (25.8)	110.79	102.60-119.65
C_{max} (pg/mL)	1942.1 2028.1 (37.1)	1563.8 1623.3 (28.9)	124.19	105.85-145.71
T_{max}§ (h)	1.17	1.25		
$T_{½}$€ (h)	2.65 (32.2)	2.30 (37.3)		

* pms-NABILONE, Pharmascience Inc., Montreal, Quebec, Canada
† Cesamet®, Valeant Canada Ltée/Ltd., Montreal, Quebec, Canada
§ Expressed as the median (range) only
€ Expressed as the arithmetic mean (CV%) only

INDICATIONS

Adults: > 18 years
pms-NABILONE (nabilone) is indicated for the management of severe nausea and vomiting associated with cancer chemotherapy.

Pediatrics: < 18 years
The safety and efficacy of pms-NABILONE in the pediatric population have not been established and its use is not recommended in this patient population.

Geriatrics: > 65 years
pms-NABILONE should be used with caution in the elderly. (See PRECAUTIONS).

CONTRAINDICATIONS

Nabilone is contraindicated in patients with known sensitivity to marijuana or other cannabinoid agents, and in those with a history of psychotic reactions.

WARNINGS

Nabilone should be used with extreme caution in patients with severe liver dysfunction and in those with a history of non-psychotic emotional disorders.

Nabilone should not be taken with alcohol, sedatives, hypnotics, or other psychotomimetic substances.

Nabilone should not be used during pregnancy, in nursing mothers, or pediatric patients since its safety under these conditions has not been established.

PRECAUTIONS

Since nabilone will often impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a car and operating machinery, the patient should be warned accordingly and should not be permitted to drive or engage in dangerous tasks until the effects of nabilone are no longer present.

Adverse psychotropic reactions can persist for 48 to 72 hours following cessation of treatment.

Since nabilone elevates supine and standing heart rates and causes postural hypotension, it should be used with caution in the elderly and in patients with hypertension or heart disease.

Drug Interactions: Potential interactions between nabilone, and diazepam; sodium secobarbital; alcohol; or codeine, were evaluated. The depressant effects of the combinations were additive. Psychomotor function was particularly impaired with concurrent use of diazepam.

Pediatric Use: The safety and efficacy in children under the age of 18 has not been established. Therefore the use of nabilone in this patient population is not recommended.

ADVERSE REACTIONS

The most frequently observed adverse reactions to nabilone and their incidences reported in the course of clinical trials were as follows: drowsiness (66.0%), vertigo (58.8%), psychological high (38.8%), dry mouth (21.6%), depression (14.0%), ataxia (12.8%), blurred vision (12.8%), sensation disturbance (12.4%), anorexia (7.6%), asthenia (7.6%),

headache (7.2%), orthostatic hypotension (5.2%), euphoria (4.0%) and hallucinations (2.0%).

The following adverse reactions were observed in less than 1% of the patients who were administered nabilone in the course of the clinical trials: tachycardia, tremors, syncope, nightmares, distortion in the perception of time, confusion, dissociation, dysphoria, psychotic reactions and seizures.

Spontaneously Reported Adverse Reactions: The following adverse reactions listed in order of decreasing frequency by body system have been reported since nabilone has been marketed. All events are listed regardless of causality assessment.

Blood and Hematopoetic: Leukopenia

Cardiovascular: Hypotension and tachycardia

Eye and Ear: Visual disturbances

Gastrointestinal: Dry mouth, nausea, vomiting, and constipation

Nervous System: Hallucinations, CNS depression, CNS stimulation, ataxia, stupor, vertigo, convulsion, and circumoral paresthesia

Psychiatric: Somnolence, confusion, euphoria, depression, dysphoria, depersonalization, anxiety, psychosis, and emotional lability

Miscellaneous and Ill-Defined Conditions: Dizziness, headache, insomnia, abnormal thinking, chest pain, lack of effect, and face edema

SYMPTOMS AND TREATMENT OF OVERDOSE

Signs and Symptoms: Signs and symptoms which might be expected to occur are psychotic episodes including hallucinations, anxiety reactions, respiratory depression and coma (experience with cases of overdosage of more than 10 mg/day has not yet been reported).

Treatment: Overdosage may be considered to have occurred, even at prescribed dosages, if disturbing psychiatric symptoms are present. In these cases, the patient should be observed in a quiet environment and supportive measures, including reassurance, should be used. Subsequent doses should be withheld until patients have returned to their baseline mental status; routine dosing may then be resumed if clinically indicated. In such instances, a lower initiating dose is suggested.

If psychotic episodes occur, the patient should be managed conservatively, if possible. For moderate psychotic episodes and anxiety reactions, verbal support and comforting may be sufficient. In more severe cases, antipsychotic drugs may be useful; however, the

utility of antipsychotic drugs in cannabinoid psychosis has not been systematically evaluated. Support for their use is drawn from limited experience using antipsychotic agents to manage cannabis overdoses. Because of the potential for drug-drug interactions (eg, additive CNS depressant effects due to nabilone and chlorpromazine), such patients should be closely monitored.

Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which, in many cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal.

The use of forced diuresis, peritoneal dialysis, hemodialysis, charcoal hemoperfusion, or cholestyramine has not been reported. In the presence of normal renal function, most of a dose of nabilone is eliminated through the biliary system.

Treatment for respiratory depression and comatose state consists in symptomatic and supportive therapy. Particular attention should be paid to the occurrence of hypothermia. If the patient becomes hypotensive, consider fluids, inotropes, and/or vasopressors.

For management of a suspected drug overdose, contact your regional Poison Control Centre immediately.

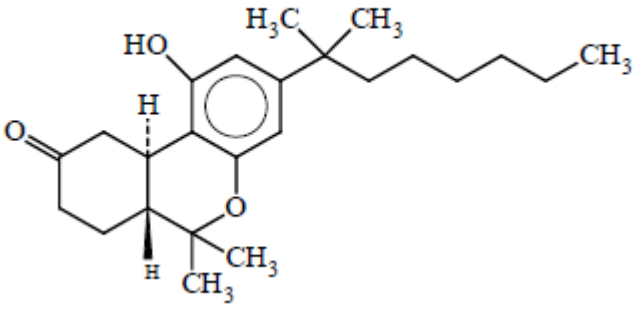
DOSAGE AND ADMINISTRATION

Adults:
The usual dosage of pms-NABILONE (nabilone) is 1 mg or 2 mg twice a day. The first dose should be given the night before initiating administration of chemotherapeutic medication. The second dose is usually administered 1 to 3 hours before chemotherapy. If required, administration of pms-NABILONE can be continued up to 24 hours after the chemotherapeutic agent is given. The maximum recommended daily dose is 6 mg in divided doses.

pms-NABILONE is available in 0.25 mg and 0.5 mg strengths for dose adjustment within the therapeutic range. Dose adjustment may be required for the purposes of response and tolerance in individual patients. Overdosage may occur even at prescribed dosages, if disturbing psychiatric symptoms are present. In these cases, the patient should be observed in a quiet environment and supportive measures, including reassurance, should be used. Subsequent doses should be withheld until patients have returned to their baseline mental status; routine dosing may then be resumed if clinically indicated. In such instances, a lower initiating dose is suggested.

pms-NABILONE contains nabilone in a capsule dosage form and is intended only for oral administration.

STRUCTURAL FORMULA AND CHEMISTRY



Molecular Formula: $C_{24}H_{36}O_3$

Molecular Weight: 372 g/mol

U.S.A.N: Nabilone

Chemical Name: trans(+)-3-(1,1-dimethylheptyl)-6,6a,7,8,10,10a-hexahydro-1-hydroxy-6, 6-dimethyl-9H-dibenzo(b,d),pyran-9-one

Description: White crystalline powder

Composition:
Each 1 mg pms-NABILONE capsule contains: 1 mg of nabilone. The inactive ingredients are: FD&C blue #2, gelatin, pre-gelatinized starch, povidone, red iron oxide and titanium dioxide.

Each 0.5 mg pms-NABILONE capsule contains: 0.5 mg of nabilone. The inactive ingredients are: D&C red # 33, D&C yellow # 10, FD&C red # 40, gelatin, pre-gelatinized starch, povidone, titanium dioxide.

Each 0.25 mg pms-NABILONE capsule contains: 0.25 mg of nabilone. The inactive ingredients are: D&C yellow # 10, FD&C blue #1, FD&C red # 40, gelatin, pre-gelatinized starch, povidone, titanium dioxide.

Stability and Storage Recommendations:
Store at controlled room temperature at 15-30°C.

AVAILABILITY

pms-NABILONE (nabilone) capsules:

1 mg: each No. 2 hard gelatin capsule, opaque blue cap and white body, imprinted "NB" on the cap and "1" on the body, contains 1 mg of nabilone and are available in bottles of 50 capsules and 100 capsules.

0.5 mg: each No. 4 hard gelatin capsule, opaque red cap and white body, imprinted "NB" on the cap and "0.5" on the body, contains 0.5 mg of nabilone and are available in bottles of 50 and 100 capsules.

0.25 mg: each No. 4 hard gelatin capsule, opaque green cap and white body, imprinted "NB" on the cap and "0.25" on the body, contains 0.25 mg of nabilone and are available in bottles of 50.

pms-NABILONE legally is considered to be a narcotic and is subject to the controls which apply to those drugs.

PHARMACOLOGY

Nabilone has neurologic, endocrinologic and cardiovascular activity in animals although these may not be valid predictors of effects in a clinical setting.

Nabilone produces ataxia and hypoactivity; by the oral route, it is twice as active as Δ^9 THC. In rabbits and in rhesus monkeys, doses of 0.064 and 0.01 mg/kg, respectively, caused a modest decrease in blood pressure. Massive doses of 3 mg/kg caused sustained, alternating periods of hypotension and hypertension in rhesus monkeys. Doses of 0.064 mg/kg in dogs caused a modest, delayed increase in blood pressure.

Standard behavioural assays were used to evaluate psychoactive effects. Nabilone slowed muricidal activity in rats, reduced reactivity of septal-lesioned rats, slowed self-stimulation, reduced food consumption and increased reactivity to touch. In most operant conditioning studies nabilone depressed responding.

Nabilone effectively antagonized emetic doses of carmustine and of mechlorethamine in cats. Naloxone antagonized the anti-emetic effect of nabilone in apomorphine or deslanoside-induced emesis in cats.

Nabilone is rapidly absorbed and extensively metabolized in rats, dogs, monkeys and man.

Two major metabolic pathways appear to be involved in the bio-transformation of nabilone. One is the stereo-specific enzymatic reduction of nabilone to two metabolites, the RRS and the SSS carbinols. A second possible metabolic pathway is the direct

enzymatic oxidation of the aliphatic side-chain of nabilone, without prior reduction of the 9-keto moiety, to produce hydroxylic and carboxylic analogs.

In the dog, the stereo-specific reduction pathway appears to be the more important, and possibly the only, pathway involved. This probability is supported by the high concentrations of the SSS carbinol metabolite found in dog plasma and brain tissue, as compared to those concentrations found in monkeys.

In the dog, peak plasma concentrations of nabilone and of the SSS metabolite occurred two hours after an oral dose. Carbinol levels were 3 to 4 times greater than those of nabilone, and the combined concentrations accounted for essentially all of the plasma radiocarbon. The concentration of the SSS carbinol in brain tissue was 2 to 4 times greater than that found in plasma. The plasma half-life of nabilone was approximately 2 hours, while that of the radiocarbon and of the metabolite was over 30 hours. Furthermore, after repeated dosing, the SSS carbinol accumulated in brain tissue in the dog, but not in the monkey. It is thought that the presence of these high concentrations of metabolite in plasma and brain over time may have played a role in the toxicity of nabilone observed in the long-term canine study.

In the monkey, the kinetics of nabilone are different from the dog but similar to those in man (see ACTION section). Furthermore, in the monkey and in man, the two metabolic pathways appear to be involved, the more important one also being direct enzymatic oxidation.

Antiemetic Effects of Nabilone in Animals:
The antiemetic activity of nabilone was evaluated in cats against carmustine (BCNU) and mechlorethamine (HN2). Without pretreatment, BCNU at 10 to 20 mg/kg evoked vomiting with an incidence of 50 percent (11 of 22 trials) and an average latency of 145 minutes. In contrast, after pretreatment with nabilone, BCNU failed to cause vomiting in any of 14 trials. HN2 at 5 mg/kg proved to elicit vomiting uniformly and promptly, with an average latency of 15 minutes. In the presence of nabilone, HN2 elicited vomiting in only 2 of 8 trials after the prolonged average latency of 209 minutes.

Nabilone is effective in reducing cis-platinin induced emesis of pigeons. Doses as low as 0.02 mg/kg, I.M., decreased the emetic episodes induced by a dose of 8 mg/kg, I.V., of cis-platinin. Nabilone is approximately 80 to 160 times more potent than prochlorperazine in this test system. Prochlorperazine effectively blocks apomorphine-induced emesis at doses of 0.125, 0.25 and 0.5 mg/kg, I.V. Nabilone, on the other hand, was totally ineffective in blocking apomorphineinduced emesis at doses of 0.008, 0.016 and 0.032 mg/kg, I.V.

HUMAN PHARMACOLOGY

Radiolabeled ^{14}C-nabilone formulated with PVP was administered orally to two fasted subjects in a 2 mg dose containing 48 μCi of radioactivity. The plasma concentration of ^{14}C-nabilone equivalence reached approximately 10 ng/mL at 1 to 2 hours and then

disappeared exponentially with time. After the oral administration of the ^{14}C-nabilone-PVP formulation, 60 percent of the radioactivity was recovered in feces and 24 percent was recovered in urine for a total recovery of 84 percent.
Intravenous studies were conducted with a solution obtained by dissolving nabilone in ethanol. A 0.5 mg intravenous dose of ^{14}C -labeled nabilone administered to 5 normal subjects resulted in a mean area under the plasma concentration curve of 90 ng/hr/mL. Approximately 22 percent of the radioactivity was recovered in urine and approximately 67 percent was recovered in feces.

Less than 1 percent was recovered as expired CO_2.

The mean area under the plasma concentration curve after a 2 mg oral dose in two subjects was 345 ng/hr/mL. The percentages of radioactivity excreted in urine and feces after the oral and intravenous administration of nabilone are in good agreement.

This supports the view that most of the oral dose was absorbed. The results further indicate that within the dose range studied, the elimination of the drug was independent of the route of administration and the size of the dose.

^{14}C-nabilone (0.5 mg, 12 μCi) was administered by the intravenous route to 5 subjects. Plasma concentration of total radioactivity disappeared after dosing in at least a biphasic manner with the initial phase representing uptake and distribution into tissues, while the latter phase presumably represented metabolism and subsequent excretion of the drug.

The alcoholic metabolite forms rapidly and disappears at a slower rate than the parent compound. The mean plasma half life of total radioactivity for the five subjects was 20.6 ±1.3 hours over a range of 17 to 25 hours.

Chronic oral administration of nabilone 1 mg t.i.d. for 14 days resulted in no significant accumulation of nabilone or carbinol.

TOXICOLOGY

Acute Toxicity:
The oral LD_{50} of nabilone was >1000 mg/kg in mice, >2000 mg/kg in rats, >1 mg/kg in cats and >5 mg/kg in monkeys. The oral and intravenous LD50 in dogs was higher than 1 mg/kg. Signs of toxicity included hypoactivity, ataxia and respiratory depression in all species. Dogs given singly intravenous doses of 1 mg/kg promptly became ataxic and lost consciousness for about 48 hours.

Subacute Toxicity:
Rats: Nabilone was administered to rats for 14 consecutive days, at a dose of 0.8 mg/kg, by the intravenous route. Two animals died during the study. Effects seen after dosing included loss of righting reflex, intermittent tonic convulsions, hypnosis, vocalization, Straub tail and hypothermia.

Nabilone was administered in the diet to rats for 92 days, at dosage levels of 6.25, 12.50 and 25.00 mg/kg. Hypothermia was observed in all treated animals during the first 24 hours. During the first week, catatonia and hyperirritability to touch occurred in the high-dose group. Slight to moderate decreases in body weight gains occurred in all treated groups.

Dogs: Intravenous doses of 0.4 mg/kg/day were administered to dogs for 14 days. Effects observed after dosing included hyperirritability to touch, sedation, respiratory depression, fine tremors, ataxia and anorexia. All dogs developed thrombophlebitis at the injection site.

Nabilone also was administered orally for 3 months at dose levels of 0.25, 0.5, and 1.0 mg/kg/day. During the first week, ataxia was seen in the mid and high-dose group and anorexia in the high-dose group.

Chronic Toxicity:
A year-long study in dogs was initiated, but terminated after 7 months due to high mortality. Nabilone was administered orally at dose levels of 0.5, 1.0 and 2.0 mg/kg/day. Eight dogs per dose were treated. Most deaths were preceded by convulsions. No histopathologic lesions were found in the brain or other tissues. The occurrence of convulsions and death in these dogs was believed to be due to the accumulation of a toxic metabolite in the plasma and the brain.

A subacute study in which the toxicity of nabilone was compared to that of SSS carbinol was conducted in dogs. Nabilone and the SSS carbinol were administered daily for five days, intravenously, to 1 male and 1 female per drug, at the dose of 2 mg/kg. One nabilone-treated dog became moribund and was sacrificed on the second day. Anorexia, ataxia, hypoactivity, emesis and shivering were observed in both treated groups. Plasma levels of the SSS carbinol were 27 - 37 times higher than the levels of nabilone. No convulsions occurred. Tissue levels of the SSS carbinol or of nabilone in the brain were not determined.

Doses of 0.0, 0.1, 0.5, and 2.0 mg/kg/day of nabilone were administered by the nasogastric route to Rhesus monkeys for one year. An additional group was given 2.0 mg/kg/day on an intermittent schedule: two-week periods of treatment each followed by an interval of two weeks of treatment. The only changes noted were hypoactivity and sedation which occurred the first two days at the mid- and high-dose levels. Transient periods of anorexia and isolated instances of ataxia and emesis also were noted at the high-dose level.

Teratogenic Studies:
Nabilone was administered orally to pregnant rats on gestation days 6 through 15 at doses of 1, 4 and 12 mg/kg. Hypoactivity and, when handled, hyperirritability and hypertonia were observed during the first three days of treatment. Anorexia and weight loss occurred in all treated groups. Litter size was decreased and resorption incidences increased. The body weights of fetuses from treated animals were slightly reduced.

Nabilone was administered orally to gravid rabbits on gestation days 6 through 18 of 0.7, 1.6 and 3.3 mg/kg. Anorexia and decreased body weight occurred in the mid- and high-dose groups. One rabbit each in the low- and mid-dose groups. and three rabbits in the high-dose, aborted and resorption incidences were increased at the mid- and high-dose levels.

Reproduction Studies:
Nabilone was administered in the diet to rats at dose levels of 1, 4 and 12 mg/kg. Male and female rats were treated, respectively, for 60 and 17 days prior to mating; in females, nabilone administration continued through mating, gestation and lactation periods. Dose-related decrease in body weight and food consumption occurred in both male and female rats. The mean liveborn litter size in the high-dose group was decreased due to increased number of stillborn.

Perinatal and Postnatal Studies:
Nabilone was administered by gavage to pregnant rats at doses of 1, 4 and 12 mg/kg from gestation day 14 through post-partum day 21. Maternal food intake and body weight gain were decreased in treated dams. Mean litter size and survival values were significantly decreased in the high-dose group: only 4 litters survived through post-partum day 7 and the remainder of the study. Progeny survival in the mid-dose group was slightly decreased. The initial body weights of pups in the mid- and high-dose groups were depressed, and hypothermia was observed in pups from the high-dose group.

Dominant-Lethal Tests in Rats:
Two studies were conducted using the nabilone-PVP co-precipitate, the results were not indicative of a dominant- lethal effect.

Micronucleus Test:
There was no treatment-related effect on the incidence of micronuclei in rat bone marrow polychromatic erythrocytes.

Hypothermia in Rats:
Nabilone produced hypothermia in rats, the response was not significantly altered by differences in the age, sex, or nutritional status of the nabilone-treated rats.

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PART III: CONSUMER INFORMATION

[N] pms-NABILONE
Nabilone Capsules

This leaflet is part III of a three-part "Product Monograph" published when pms-NABILONE was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about pms-NABILONE. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
pms-NABILONE (nabilone) is indicated for the management of severe nausea and vomiting associated with cancer therapy.

What it does:
pms-NABILONE decreases nausea (sensation of feeling sick) and vomiting.

When it should not be used:
- You should not take pms-NABILONE if:
- you have known sensitivity to marijuana or other cannabinoid agents
- you have a history of psychotic reactions
- you are under the age of 18 years
- you are breastfeeding
- you are pregnant

What the medicinal ingredient is:
The medicinal ingredient in pms-NABILONE is nabilone, a synthetic cannabinoid agent.

What the non-medicinal ingredients are:
D&C red #33 (0.5 mg capsule), D&C yellow #10 (0.25 and 0.5 mg capsules), FD&C blue #1 (0.25 mg capsule), FD&C blue #2 (1 mg capsule), FD&D red #40 (0.25 and 0.5 mg capsules), gelatin, iron oxide red (1 mg capsule), pre-gelatinised starch, povidone, and titanium dioxide.

What dosage forms it comes in:
Capsules : 0.25 mg, 0.5 mg, and 1 mg

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Since pms-NABILONE will often impair the mental and/or physical abilities required for the performance of potentially hazardous task, you should not drive a car, operate machinery, or perform any activity that requires mental alertness until the effects of pms-NABILONE are no longer present.
- While taking pms-NABILONE, do not drink alcohol or take other drugs such as sedatives, hypnotics or other substances that can affect the nervous system without consulting with your doctor.
- pms-NABILONE should be used with extreme caution if you have severe liver dysfunction or a history of non-psychotic emotional disorders.

BEFORE you use pms-NABILONE talk to your doctor or pharmacist if:
- you are taking any other prescription or non-prescription medicine, or natural/herbal remedies
- you are pregnant or breastfeeding
- you are allergic to nabilone, the main ingredient in pms-NABILONE , or any other ingredient in pms-NABILONE (see"What the non-medicinal ingredients are")
- you have hypertension or heart problems

INTEARCTIONS WITH THIS MEDICATION

While you are taking pms-NABILONE, do not start any new medicines, including natural or herbal medicines, without speaking to your doctor first. Tell your doctor about all the medicines that you are taking including those that you have bought yourself.

pms-NABILONE can interact with:
- Diazepam
- Sodium secobarbital
- Alcohol
- Codeine
- Any medicine that affects your mental and psychomotor function (e.g., causes hallucinations, weird thoughts, etc).

PROPER USE OF THIS MEDICATION

The label on the container of your medicine should tell you how often to take your medicine and how many doses you should take each time. If not, or if you are not sure, ask your doctor or pharmacist.

Do not take more doses, or take them more often than your doctor prescribes.
Your doctor prescribed pms-NABILONE for your use only. You should not let anyone else use it.

Usual adult dose:
You will receive pms-NABILONE prior to chemotherapy and, if necessary, after cancer treatment. Based on how likely you are to experience nausea and/or vomiting, caused by your cancer treatment, your doctor will tell you the amount you need to take and how frequently. Follow the directions provided by your doctor for using this medicine. Your doctor may also have to adjust your dose depending on how you react to pms-NABILONE.

Overdose:
Some of the signs of overdose are psychotic episodes including hallucinations, anxiety reactions, respiratory depression, and coma.

Overdose may even occur at prescribed doses. If psychiatric symptoms (e.g., weird thoughts, hallucinations, etc.) are present, contact poison control centre immediately or go to the nearest emergency room.

Missed Dose:
If you forget a dose of pms-NABILONE, you should take it as soon as you remember. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. **Do not** double your dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Some patients may experience drowsiness, psychological high, vertigo, dry mouth, depression, ataxia, asthenia, blurred vision, sensation disturbance, anorexia, headache, orthostatic hypotension, euphoria, and hallucinations. You should tell your doctor or pharmacist about these symptoms.

If your nausea (feeling of sickness) or vomiting do not improve while taking pms-NABILONE, consult your doctor for further advice.

If you feel unwell or have any symptoms that you do not understand, you should contact your doctor immediately.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom/effect		Talk with your doctor or pharmacist		Stop taking drug and seek emergency medical assistance
		Only if severe	In all cases	
Common	Drowsiness		✓	
	Dry mouth	✓		
	Euphoria		✓	
	Hallucinations			✓
	Somnolence		✓	
	Vertigo		✓	
Uncommon	Confusion			✓
	Depression		✓	
	Dissociation			✓
	Headache	✓		
	Orthostatic hypotension		✓	
	Nightmares		✓	
	Seizure			✓
	Tachycardia		✓	
	Tremors		✓	

This is not a complete list of side effects. For any unexpected effects while taking pms-NABILONE, contact your doctor or pharmacist immediately.

HOW TO STORE IT

Keep pms-NABILONE out of reach of children.
Store it at room temperature (15 to 30°C) in the package it came in.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Reporting Suspected Side Effects
You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to:
    Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be obtained by contacting the sponsor, Pharmascience Inc. at: 1-888-550-6060

This leaflet was prepared by.

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