This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda



500012 Rev Sep 2004

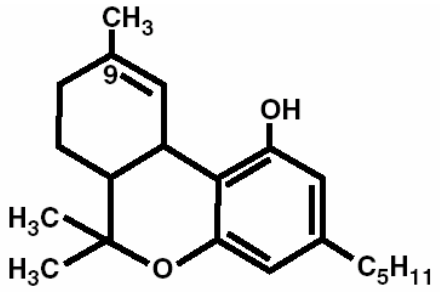
# MARINOL® CIII

**(Dronabinol)**
**Capsules**

$R_x$ only

## DESCRIPTION

Dronabinol is a cannabinoid designated chemically as (6*aR-trans*)-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-6*H*-dibenzo[*b,d*]pyran-1-ol. Dronabinol has the following empirical and structural formulas:




$C_{21}H_{30}O_2$ (molecular weight = 314.47)

Dronabinol, the active ingredient in MARINOL® Capsules, is synthetic delta-9-tetrahydrocannabinol (delta-9-THC). Delta-9-tetrahydrocannabinol is also a naturally occurring component of *Cannabis sativa L.* (Marijuana).

Dronabinol is a light yellow resinous oil that is sticky at room temperature and hardens upon refrigeration. Dronabinol is insoluble in water and is formulated in sesame oil. It has a pKa of 10.6 and an octanol-water partition coefficient: 6,000:1 at pH 7.

Capsules for oral administration: MARINOL® Capsules is supplied as round, soft gelatin capsules containing either 2.5 mg, 5 mg, or 10 mg dronabinol. Each MARINOL® Capsule is formulated with the following inactive ingredients: FD&C Blue No. 1 (5 mg), FD&C Red No. 40 (5 mg), FD&C Yellow No. 6 (5 mg and 10 mg), gelatin, glycerin, methylparaben, propylparaben, sesame oil, and titanium dioxide.

## CLINICAL PHARMACOLOGY

Dronabinol is an orally active cannabinoid which, like other cannabinoids, has complex effects on the central nervous system (CNS), including central sympathomimetic activity. Cannabinoid receptors have been discovered in neural tissues. These receptors may play a role in mediating the effects of dronabinol and other cannabinoids.

### Pharmacodynamics

Dronabinol-induced sympathomimetic activity may result in tachycardia and/or conjunctival injection. Its effects on blood pressure are inconsistent, but occasional subjects have experienced orthostatic hypotension and/or syncope upon abrupt standing.



HELSINN EXHIBIT 2042
Azurity Pharmaceuticals, Inc. v. Helsinn Healthcare S.A.
IPR2025-00945

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda



Dronabinol also demonstrates reversible effects on appetite, mood, cognition, memory, and perception. These phenomena appear to be dose-related, increasing in frequency with higher dosages, and subject to great interpatient variability.

After oral administration, dronabinol has an onset of action of approximately 0.5 to 1 hours and peak effect at 2 to 4 hours. Duration of action for psychoactive effects is 4 to 6 hours, but the appetite stimulant effect of dronabinol may continue for 24 hours or longer after administration.

Tachyphylaxis and tolerance develop to some of the pharmacologic effects of dronabinol and other cannabinoids with chronic use, suggesting an indirect effect on sympathetic neurons. In a study of the pharmacodynamics of chronic dronabinol exposure, healthy male volunteers (N = 12) received 210 mg/day dronabinol, administered orally in divided doses, for 16 days. An initial tachycardia induced by dronabinol was replaced successively by normal sinus rhythm and then bradycardia. A decrease in supine blood pressure, made worse by standing, was also observed initially. These volunteers developed tolerance to the cardiovascular and subjective adverse CNS effects of dronabinol within 12 days of treatment initiation.

Tachyphylaxis and tolerance do not, however, appear to develop to the appetite stimulant effect of MARINOL® Capsules. In studies involving patients with Acquired Immune Deficiency Syndrome (AIDS), the appetite stimulant effect of MARINOL® Capsules has been sustained for up to five months in clinical trials, at dosages ranging from 2.5 mg/day to 20 mg/day.

**Pharmacokinetics**

***Absorption and Distribution:*** MARINOL® (Dronabinol) Capsules is almost completely absorbed (90 to 95%) after single oral doses. Due to the combined effects of first pass hepatic metabolism and high lipid solubility, only 10 to 20% of the administered dose reaches the systemic circulation. Dronabinol has a large apparent volume of distribution, approximately 10 L/kg, because of its lipid solubility. The plasma protein binding of dronabinol and its metabolites is approximately 97%.

The elimination phase of dronabinol can be described using a two compartment model with an initial (alpha) half-life of about 4 hours and a terminal (beta) half-life of 25 to 36 hours. Because of its large volume of distribution, dronabinol and its metabolites may be excreted at low levels for prolonged periods of time.

The pharmacokinetics of dronabinol after single doses (2.5, 5, and 10 mg) and multiple doses (2.5, 5, and 10 mg given twice a day; BID) have been studied in healthy women and men.

**Summary of Multiple-Dose Pharmacokinetic Parameters of Dronabinol in Healthy Volunteers (n=34; 20-45 years) under Fasted Conditions**

| Mean (SD) PK Parameter Values | | | |
|---|---|---|---|
| **BID Dose** | **Cmax ng/mL** | **Median Tmax (range), hr** | **AUC(0-12) ng•hr/mL** |
| 2.5 mg | 1.32 (0.62) | 1.00 (0.50-4.00) | 2.88 (1.57) |
| 5 mg | 2.96 (1.81) | 2.50 (0.50-4.00) | 6.16 (1.85) |
| 10 mg | 7.88 (4.54) | 1.50 (0.50-3.50) | 15.2 (5.52) |

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda



A slight increase in dose proportionality on mean Cmax and AUC (0-12) of dronabinol was observed with increasing dose over the dose range studied.

***Metabolism:*** Dronabinol undergoes extensive first-pass hepatic metabolism, primarily by microsomal hydroxylation, yielding both active and inactive metabolites. Dronabinol and its principal active metabolite, 11-OH-delta-9-THC, are present in approximately equal concentrations in plasma. Concentrations of both parent drug and metabolite peak at approximately 0.5 to 4 hours after oral dosing and decline over several days. Values for clearance average about 0.2 L/kg-hr, but are highly variable due to the complexity of cannabinoid distribution.

***Elimination:*** Dronabinol and its biotransformation products are excreted in both feces and urine. Biliary excretion is the major route of elimination with about half of a radio-labeled oral dose being recovered from the feces within 72 hours as contrasted with 10 to 15% recovered from urine. Less than 5% of an oral dose is recovered unchanged in the feces.

Following single dose administration, low levels of dronabinol metabolites have been detected for more than 5 weeks in the urine and feces.

In a study of MARINOL® Capsules involving AIDS patients, urinary cannabinoid/creatinine concentration ratios were studied bi-weekly over a six week period. The urinary cannabinoid/creatinine ratio was closely correlated with dose. No increase in the cannabinoid/creatinine ratio was observed after the first two weeks of treatment, indicating that steady-state cannabinoid levels had been reached. This conclusion is consistent with predictions based on the observed terminal half-life of dronabinol.

***Special Populations:*** The pharmacokinetic profile of MARINOL® Capsules has not been investigated in either pediatric or geriatric patients.

## Clinical Trials

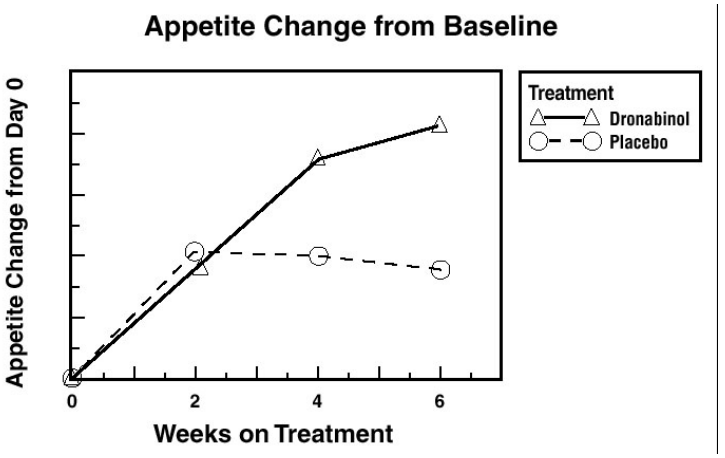
***Appetite Stimulation:*** The appetite stimulant effect of MARINOL® (Dronabinol) Capsules in the treatment of AIDS-related anorexia associated with weight loss was studied in a randomized, double-blind, placebo-controlled study involving 139 patients. The initial dosage of MARINOL® Capsules in all patients was 5 mg/day, administered in doses of 2.5 mg one hour before lunch and one hour before supper. In pilot studies, early morning administration of MARINOL® Capsules appeared to have been associated with an increased frequency of adverse experiences, as compared to dosing later in the day. The effect of MARINOL® Capsules on appetite, weight, mood, and nausea was measured at scheduled intervals during the six-week treatment period. Side effects (feeling high, dizziness, confusion, somnolence) occurred in 13 of 72 patients (18%) at this dosage level and the dosage was reduced to 2.5 mg/day, administered as a single dose at supper or bedtime.

As compared to placebo, MARINOL® Capsules treatment resulted in a statistically significant improvement in appetite as measured by visual analog scale (see figure). Trends toward improved body weight and mood, and decreases in nausea were also seen.

After completing the 6-week study, patients were allowed to continue treatment with MARINOL® Capsules in an open-label study, in which there was a sustained improvement in appetite.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda






***Antiemetic:*** MARINOL® (Dronabinol) Capsules treatment of chemotherapy-induced emesis was evaluated in 454 patients with cancer, who received a total of 750 courses of treatment of various malignancies. The antiemetic efficacy of MARINOL® Capsules was greatest in patients receiving cytotoxic therapy with MOPP for Hodgkin's and non-Hodgkin's lymphomas. MARINOL® Capsules dosages ranged from 2.5 mg/day to 40 mg/day, administered in equally divided doses every four to six hours (four times daily). As indicated in the following table, escalating the MARINOL® Capsules dose above 7 mg/m$^2$ increased the frequency of adverse experiences, with no additional antiemetic benefit.

**MARINOL® Capsules Dose: Response Frequency and Adverse Experiences***
(N = 750 treatment courses)

| **MARINOL® Capsules Dose** | **Response Frequency (%)** | | | **Adverse Events Frequency (%)** | | |
|---|---|---|---|---|---|---|
| | Complete | Partial | Poor | None | Nondysphoric | Dysphoric |
| <7 mg/m$^2$ | 36 | 32 | 32 | 23 | 65 | 12 |
| >7 mg/m$^2$ | 33 | 31 | 36 | 13 | 58 | 28 |

*Nondysphoric events consisted of drowsiness, tachycardia, etc.

Combination antiemetic therapy with MARINOL® Capsules and a phenothiazine (prochlorperazine) may result in synergistic or additive antiemetic effects and attenuate the toxicities associated with each of the agents.

## INDIVIDUALIZATION OF DOSAGES

The pharmacologic effects of MARINOL® (Dronabinol) Capsules are dose-related and subject to considerable interpatient variability. Therefore, dosage individualization is critical in achieving the maximum benefit of MARINOL® Capsules treatment.

***Appetite Stimulation:*** In the clinical trials, the majority of patients were treated with 5 mg/day MARINOL® Capsules, although the dosages ranged from 2.5 to 20 mg/day. For an adult:

1. Begin with 2.5 mg before lunch and 2.5 mg before supper. If CNS symptoms (feeling high, dizziness, confusion, somnolence) do occur, they usually resolve in 1 to 3 days with continued dosage.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda



2. If CNS symptoms are severe or persistent, reduce the dose to 2.5 mg before supper. If symptoms continue to be a problem, taking the single dose in the evening or at bedtime may reduce their severity.

3. When adverse effects are absent or minimal and further therapeutic effect is desired, increase the dose to 2.5 mg before lunch and 5 mg before supper or 5 and 5 mg. Although most patients respond to 2.5 mg twice daily, 10 mg twice daily has been tolerated in about half of the patients in appetite stimulation studies.

The pharmacologic effects of MARINOL® Capsules are reversible upon treatment cessation.

***Antiemetic:*** Most patients respond to 5 mg three or four times daily. Dosage may be escalated during a chemotherapy cycle or at subsequent cycles, based upon initial results. Therapy should be initiated at the lowest recommended dosage and titrated to clinical response. Administration of MARINOL® Capsules with phenothiazines, such as prochlorperazine, has resulted in improved efficacy as compared to either drug alone, without additional toxicity.

***Pediatrics:*** MARINOL® Capsules is not recommended for AIDS-related anorexia in pediatric patients because it has not been studied in this population. The pediatric dosage for the treatment of chemotherapy-induced emesis is the same as in adults. Caution is recommended in prescribing MARINOL® Capsules for children because of the psychoactive effects.

***Geriatrics:*** Caution is advised in prescribing MARINOL® Capsules in elderly patients because they are generally more sensitive to the psychoactive effects of drugs. In antiemetic studies, no difference in tolerance or efficacy was apparent in patients >55 years old.

## INDICATIONS AND USAGE

MARINOL® (Dronabinol) Capsules is indicated for the treatment of:

1. anorexia associated with weight loss in patients with AIDS; and

2. nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

## CONTRAINDICATIONS

MARINOL® (Dronabinol) Capsules is contraindicated in any patient who has a history of hypersensitivity to any cannabinoid or sesame oil.

## WARNINGS

Patients receiving treatment with MARINOL® Capsules should be specifically warned not to drive, operate machinery, or engage in any hazardous activity until it is established that they are able to tolerate the drug and to perform such tasks safely.

## PRECAUTIONS

**General:** The risk/benefit ratio of MARINOL® (Dronabinol) Capsules use should be carefully evaluated in patients with the following medical conditions because of individual variation in response and tolerance to the effects of MARINOL® Capsules.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda



MARINOL® Capsules should be used with caution in patients with cardiac disorders because of occasional hypotension, possible hypertension, syncope, or tachycardia (see **CLINICAL PHARMACOLOGY**).

MARINOL® Capsules should be used with caution in patients with a history of substance abuse, including alcohol abuse or dependence, because they may be more prone to abuse MARINOL® Capsules as well. Multiple substance abuse is common and marijuana, which contains the same active compound, is a frequently abused substance.

MARINOL® Capsules should be used with caution and careful psychiatric monitoring in patients with mania, depression, or schizophrenia because MARINOL® Capsules may exacerbate these illnesses.

MARINOL® Capsules should be used with caution in patients receiving concomitant therapy with sedatives, hypnotics or other psychoactive drugs because of the potential for additive or synergistic CNS effects.

MARINOL® Capsules should be used with caution in pregnant patients, nursing mothers, or pediatric patients because it has not been studied in these patient populations.

**Information for Patients:** Patients receiving treatment with MARINOL® (Dronabinol) Capsules should be alerted to the potential for additive central nervous system depression if MARINOL® Capsules is used concomitantly with alcohol or other CNS depressants such as benzodiazepines and barbiturates.

Patients receiving treatment with MARINOL® Capsules should be specifically warned not to drive, operate machinery, or engage in any hazardous activity until it is established that they are able to tolerate the drug and to perform such tasks safely.

Patients using MARINOL® Capsules should be advised of possible changes in mood and other adverse behavioral effects of the drug so as to avoid panic in the event of such manifestations. Patients should remain under the supervision of a responsible adult during initial use of MARINOL® Capsules and following dosage adjustments.

**Drug Interactions:** In studies involving patients with AIDS and/or cancer, MARINOL® (Dronabinol) Capsules has been co-administered with a variety of medications (e.g., cytotoxic agents, anti-infective agents, sedatives, or opioid analgesics) without resulting in any clinically significant drug/drug interactions. Although no drug/drug interactions were discovered during the clinical trials of MARINOL® Capsules, cannabinoids may interact with other medications through both metabolic and pharmacodynamic mechanisms. Dronabinol is highly protein bound to plasma proteins, and therefore, might displace other protein-bound drugs. Although this displacement has not been confirmed *in vivo*, practitioners should monitor patients for a change in dosage requirements when administering dronabinol to patients receiving other highly protein-bound drugs. Published reports of drug/drug interactions involving cannabinoids are summarized in the following table.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda



| CONCOMITANT DRUG | CLINICAL EFFECT(S) |
|---|---|
| Amphetamines, cocaine, other sympathomimetic agents | Additive hypertension, tachycardia, possibly cardiotoxicity |
| Atropine, scopolamine, antihistamines, other anticholinergic agents | Additive or super-additive tachycardia, drowsiness |
| Amitriptyline, amoxapine, desipramine, other tricyclic antidepressants | Additive tachycardia, hypertension, drowsiness |
| Barbiturates, benzodiazepines, ethanol, lithium, opioids, buspirone, antihistamines, muscle relaxants, other CNS depressants | Additive drowsiness and CNS depression |
| Disulfiram | A reversible hypomanic reaction was reported in a 28 y/o man who smoked marijuana; confirmed by dechallenge and rechallenge |
| Fluoxetine | A 21 y/o female with depression and bulimia receiving 20 mg/day fluoxetine X 4 wks became hypomanic after smoking marijuana; symptoms resolved after 4 days |
| Antipyrine, barbiturates | Decreased clearance of these agents, presumably via competitive inhibition of metabolism |
| Theophylline | Increased theophylline metabolism reported with smoking of marijuana; effect similar to that following smoking tobacco |

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Carcinogenicity studies in mice and rats have been conducted under the US National Toxicology Program (NTP). In the 2-year carcinogenicity study in rats, there was no evidence of carcinogenicity at doses up to 50 mg/kg/day, about 20 times the maximum recommended human dose on a body surface area basis. In the 2-year carcinogenicity study in mice, treatment with dronabinol at 125 mg/kg/day, about 25 times the maximum recommended human dose on a body surface area basis, produced thyroid follicular cell adenoma in both male and female mice but not at 250 or 500 mg/kg/day.

Dronabinol was not genotoxic in the Ames tests, the *in vitro* chromosomal aberration test in Chinese hamster ovary cells, and the *in vivo* mouse micronucleus test. It, however, produced a weak positive response in a sister chromatid exchange test in Chinese hamster ovary cells.

In a long-term study (77 days) in rats, oral administration of dronabinol at doses of 30 to 150 $mg/m^2$, equivalent to 0.3 to 1.5 times maximum recommended human dose (MRHD) of 90 $mg/m^2$/day in cancer patients or 2 to 10 times MRHD of 15 $mg/m^2$/day in AIDS patients, reduced ventral prostate, seminal vesicle and epididymal weights and caused a decrease in seminal fluid volume. Decreases in spermatogenesis, number of developing germ cells, and number of Leydig cells in the testis were also observed. However, sperm count, mating success and testosterone levels were not affected. The significance of these animal findings in humans is not known.

**Pregnancy:** Pregnancy Category C. Reproduction studies with dronabinol have been performed in mice at 15 to 450 $mg/m^2$, equivalent to 0.2 to 5 times maximum recommended human dose (MRHD)

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda



of 90 mg/m$^2$/day in cancer patients or 1 to 30 times MRHD of 15 mg/m$^2$/day in AIDS patients, and in rats at 74 to 295 mg/m$^2$ (equivalent to 0.8 to 3 times MRHD of 90 mg/m$^2$ in cancer patients or 5 to 20 times MRHD of 15 mg/m$^2$/day in AIDS patients). These studies have revealed no evidence of teratogenicity due to dronabinol. At these dosages in mice and rats, dronabinol decreased maternal weight gain and number of viable pups and increased fetal mortality and early resorptions. Such effects were dose dependent and less apparent at lower doses which produced less maternal toxicity. There are no adequate and well-controlled studies in pregnant women. Dronabinol should be used only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers:** Use of MARINOL® Capsules is not recommended in nursing mothers since, in addition to the secretion of HIV virus in breast milk, dronabinol is concentrated in and secreted in human breast milk and is absorbed by the nursing baby.

**Geriatric Use:** Clinical studies of MARINOL® (Dronabinol) Capsules in AIDS and cancer patients did not include the sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, increased sensitivity to psychoactive effects and of concomitant disease or other drug therapy.

## ADVERSE REACTIONS

Adverse experiences information summarized in the tables below was derived from well-controlled clinical trials conducted in the US and US territories involving 474 patients exposed to MARINOL® (Dronabinol) Capsules. Studies of AIDS-related weight loss included 157 patients receiving dronabinol at a dose of 2.5 mg twice daily and 67 receiving placebo. Studies of different durations were combined by considering the first occurrence of events during the first 28 days. Studies of nausea and vomiting related to cancer chemotherapy included 317 patients receiving dronabinol and 68 receiving placebo.

A cannabinoid dose-related "high" (easy laughing, elation and heightened awareness) has been reported by patients receiving MARINOL® Capsules in both the antiemetic (24%) and the lower dose appetite stimulant clinical trials (8%) (see **Clinical Trials**).

The most frequently reported adverse experiences in patients with AIDS during placebo-controlled clinical trials involved the CNS and were reported by 33% of patients receiving MARINOL® Capsules. About 25% of patients reported a minor CNS adverse event during the first 2 weeks and about 4% reported such an event each week for the next 6 weeks thereafter.

**PROBABLY CAUSALLY RELATED: Incidence greater than 1%.**
Rates derived from clinical trials in AIDS-related anorexia (N=157) and chemotherapy-related nausea (N=317). Rates were generally higher in the anti-emetic use (given in parentheses).

*Body as a whole:* Asthenia.
*Cardiovascular:* Palpitations, tachycardia, vasodilation/facial flush.
*Digestive:* Abdominal pain*, nausea*, vomiting*.
*Nervous system:* (Amnesia), anxiety/nervousness, (ataxia), confusion, depersonalization, dizziness*, euphoria*, (hallucination), paranoid reaction*, somnolence*, thinking abnormal*.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda



*Incidence of events 3% to 10%

**PROBABLY CAUSALLY RELATED: Incidence less than 1%.**
Event rates derived from clinical trials in AIDS-related anorexia (N=157) and chemotherapy-related nausea (N=317).

*Cardiovascular:* Conjunctivitis*, hypotension*.
*Digestive:* Diarrhea*, fecal incontinence.
*Musculoskeletal:* Myalgias.
*Nervous system:* Depression, nightmares, speech difficulties, tinnitus.
*Skin and Appendages:* Flushing*.
*Special senses:* Vision difficulties.

*Incidence of events 0.3% to 1%

**CAUSAL RELATIONSHIP UNKNOWN: Incidence less than 1%.**
The clinical significance of the association of these events with MARINOL® Capsules treatment is unknown, but they are reported as alerting information for the clinician.

*Body as a whole:* Chills, headache, malaise.
*Digestive:* Anorexia, hepatic enzyme elevation.
*Respiratory:* Cough, rhinitis, sinusitis.
*Skin and Appendages:* Sweating.

## DRUG ABUSE AND DEPENDENCE

MARINOL® (Dronabinol) Capsules is one of the psychoactive compounds present in cannabis, and is abusable and controlled [Schedule III (CIII)] under the Controlled Substances Act. Both psychological and physiological dependence have been noted in healthy individuals receiving dronabinol, but addiction is uncommon and has only been seen after prolonged high dose administration.

Chronic abuse of cannabis has been associated with decrements in motivation, cognition, judgement, and perception. The etiology of these impairments is unknown, but may be associated with the complex process of addiction rather than an isolated effect of the drug. No such decrements in psychological, social or neurological status have been associated with the administration of MARINOL® Capsules for therapeutic purposes.

In an open-label study in patients with AIDS who received MARINOL® Capsules for up to five months, no abuse, diversion or systematic change in personality or social functioning were observed despite the inclusion of a substantial number of patients with a past history of drug abuse.

An abstinence syndrome has been reported after the abrupt discontinuation of dronabinol in volunteers receiving dosages of 210 mg/day for 12 to 16 consecutive days. Within 12 hours after discontinuation, these volunteers manifested symptoms such as irritability, insomnia, and restlessness. By approximately 24 hours post-dronabinol discontinuation, withdrawal symptoms intensified to include “hot flashes”, sweating, rhinorrhea, loose stools, hiccoughs and anorexia.

These withdrawal symptoms gradually dissipated over the next 48 hours. Electroencephalographic changes consistent with the effects of drug withdrawal (hyperexcitation) were recorded in patients after abrupt dechallenge. Patients also complained of disturbed sleep for several weeks after discontinuing therapy with high dosages of dronabinol.

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda



## OVERDOSAGE

Signs and symptoms following MILD MARINOL® (Dronabinol) Capsules intoxication include drowsiness, euphoria, heightened sensory awareness, altered time perception, reddened conjunctiva, dry mouth and tachycardia; following MODERATE intoxication include memory impairment, depersonalization, mood alteration, urinary retention, and reduced bowel motility; and following SEVERE intoxication include decreased motor coordination, lethargy, slurred speech, and postural hypotension. Apprehensive patients may experience panic reactions and seizures may occur in patients with existing seizure disorders.

The estimated lethal human dose of intravenous dronabinol is 30 mg/kg (2100 mg/ 70 kg). Significant CNS symptoms in antiemetic studies followed oral doses of 0.4 mg/kg (28 mg/70 kg) of MARINOL® Capsules.

**Management:** A potentially serious oral ingestion, if recent, should be managed with gut decontamination. In unconscious patients with a secure airway, instill activated charcoal (30 to 100 g in adults, 1 to 2 g/kg in infants) via a nasogastric tube. A saline cathartic or sorbitol may be added to the first dose of activated charcoal. Patients experiencing depressive, hallucinatory or psychotic reactions should be placed in a quiet area and offered reassurance. Benzodiazepines (5 to 10 mg diazepam *po*) may be used for treatment of extreme agitation. Hypotension usually responds to Trendelenburg position and IV fluids. Pressors are rarely required.

## DOSAGE AND ADMINISTRATION

**Appetite Stimulation:** Initially, 2.5 mg MARINOL® (Dronabinol) Capsules should be administered orally twice daily (b.i.d.), before lunch and supper. For patients unable to tolerate this 5 mg/day dosage of MARINOL® Capsules, the dosage can be reduced to 2.5 mg/day, administered as a single dose in the evening or at bedtime. If clinically indicated and in the absence of significant adverse effects, the dosage may be gradually increased to a maximum of 20 mg/day MARINOL® Capsules, administered in divided oral doses. Caution should be exercised in escalating the dosage of MARINOL® Capsules because of the increased frequency of dose-related adverse experiences at higher dosages (see **PRECAUTIONS**).

**Antiemetic:** MARINOL® Capsules is best administered at an initial dose of 5 mg/m$^2$, given 1 to 3 hours prior to the administration of chemotherapy, then every 2 to 4 hours after chemotherapy is given, for a total of 4 to 6 doses/day. Should the 5 mg/m$^2$ dose prove to be ineffective, and in the absence of significant side effects, the dose may be escalated by 2.5 mg/m$^2$ increments to a maximum of 15 mg/m$^2$ per dose. Caution should be exercised in dose escalation, however, as the incidence of disturbing psychiatric symptoms increases significantly at maximum dose (see **PRECAUTIONS**).

## STORAGE CONDITIONS

**MARINOL® (Dronabinol) Capsules should be packaged in a well-closed container and stored in a cool environment between 8° and 15°C (46° and 59°F) and alternatively could be stored in a refrigerator. Protect from freezing.**

## HOW SUPPLIED

**MARINOL® Capsules (dronabinol solution in sesame oil in soft gelatin capsules)**

**2.5 mg white capsules (Identified UM or RL).**

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda



NDC 0051-0021-21 (Bottle of 60 capsules).

**5 mg dark brown capsules (Identified UM or RL).**
NDC 0051-0022-11 (Bottle of 25 capsules).

**10 mg orange capsules (Identified UM or RL).**
NDC 0051-0023-21 (Bottle of 60 capsules).

MARINOL® is a registered trademark of Unimed Pharmaceuticals, Inc. and is Manufactured by Banner Pharmacaps, Inc.
High Point, NC 27265

500012 Rev Sep 2004

© 2004 Solvay Pharmaceuticals, Inc.

A Solvay Pharmaceuticals, Inc. Company
Marietta, GA 30062

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda