Dronabinol capsules are supplied as oblong, gelatin capsules containing 2.5 mg or 5 mg or 10 mg dronabinol. Each dronabinol capsule strength is formulated with the following inactive ingredients: FD&C Yellow No. 6, gelatin, glycercin, purged water, sesame oil, and titanium dioxide. The 2.5 mg and 5 mg also contain FD&C Blue No. 1 and FD&C Red No. 40. The capsules are printed with edible ink containing iron oxide black.

**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 detected 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 syncope upon abrupt standing.

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

After oral administration, dronabinol has an onset of action of approximately 0.5 to 1 hour and peak effect at 2 to 4 hours. Duration of action for psychoactive effects is 4 to 6 hours, but the antidepressant effect 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 nerves. In a study of the pharmacokinetics of dronabinol in healthy volunteers, the active male volunteers (N = 12) received 210 mg/day of dronabinol. At steady-state conditions, plasma concentrations of dronabinol were approximately 1 ng/mL 1 hour after administration, 2.6 ng/mL 2 hours after administration, and 0.8 ng/mL 6 hours after administration.

**Absorption and Distribution**

**Absorption**

Dronabinol capsules are almost completely absorbed (90% to 95%) after single oral doses. Due to the combined effects of first-pass hepatic extraction and high首过效应, a lower bioavailability of dronabinol is observed after oral administration than after intravenous administration. Dronabinol is distributed into various tissues and fluids, including brain, muscle, adipose tissue, and breast milk. It is also found in breast milk.

**Distribution**

Dronabinol distributes into breast milk, and the concentration of dronabinol in breast milk is approximately 0.5 ng/mL at steady-state conditions. Dronabinol is excreted in both feces and urine. Biliary excretion is the major route of elimination with minor amounts excreted in the feces.

**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-DHC-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 dose and decline over several days. Values for clearance average about 0.2 L/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. The mean elimination half-life is approximately 10 hours. The urinary cannabinoid/(creatinine concentration ratios were studied bi-weekly over a six week period. The correlation coefficients were approximately 0.8 for the cannabinoid/creatinine and cannabinoid/(urine creatinine) ratios. 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 time-halflife of the cannabinoid.

**Special Populations**

The pharmacokinetic profile of dronabinol has not been investigated in pediatric or geriatric patients.

**CLINICAL TRIALS**

**Antiemetic: Dronabinol treatment of chemotherapy-induced emesis was evaluated in 482 patients, 75% of whom had received prior treatment of various malignancies. The antiemetic efficacy of dronabinol was greater than placebo and comparable to prochlorperazine in treating cGVHD and non-Hodgkin's lymphomas. Dronabinol capsules dosages ranged from 2.5 mg/day to 45 mg/day in equally divided doses every four to five days (four to five times). As indicated in the following table, escalating the dronabinol dosage above 15 mg/day, with no more than 30 mg/day, was associated with increased frequency of adverse experiences.**

<table>
<thead>
<tr>
<th>Dronabinol Dose</th>
<th>Response Frequency and Adverse Experiences* (N = 750 treatment courses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5 mg</td>
<td>Complete: 33/31/36</td>
</tr>
<tr>
<td>5 mg</td>
<td>Partial:</td>
</tr>
<tr>
<td>10 mg</td>
<td>Poor:</td>
</tr>
</tbody>
</table>

**INDIVIDUALIZATION OF DOSAGES**

The pharmacologic effects of dronabinol are dose-related and subject to considerable individual variability. Thus, dosage should be individualized according to the response and tolerance to the effects of dronabinol.

**Antiemetic:**

Most patients respond to 5 mg three or four times daily. Dosage should be individualized to the least recommended dosage and titrated to clinical response. Administration of dronabinol capsules is affected by factors such as environmental conditions, because dronabinol is a heat labile substance.

**Pediatric: The pediatric dosage for the treatment of chemotherapy-induced nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.**

**INDICATIONS AND USAGE**

Dronabinol capsules are indicated for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

**CONTRAINDICATIONS**

Dronabinol capsules are contraindicated in any patient who has a known sensitivity to dronabinol or any of its ingredients. It contains cannabidiol and sesame oil and should never be used by patients allergic to these substances.

**WARNINGS**

Patients receiving treatment with dronabinol 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 dronabinol use should be carefully evaluated in patients with the following medical conditions because of individual variation in response and tolerance to the effects of dronabinol.

Seizure and seizure-like activity have been reported in patients receiving dronabinol capsules during marketed use of the drug and in clinical trials. (See ADVERSE REACTIONS and OVERDOSAGE.) Dronabinol capsules should be used with caution in patients with a history of seizure disorder because dronabinol capsules may lower the seizure threshold.

A causal relationship between dronabinol capsules and these events has not been established. Dronabinol capsules should be discontinued immediately in patients who develop seizures and medical attention should be sought immediately.

Dronabinol capsules should be used with caution in patients with cardiac disorders because of occasional hypotension, possible hypertension, syncope, and/or tachycardia. (See CLINICAL PHARMACOLOGY.)

Dronabinol capsules should be used with caution in patients with a history of substance abuse, including alcohol abuse or dependence, because they may have a reduced capacity to cope upon abrupt standing.

Dronabinol capsules should be used with caution in patients who are pregnant or nursing mothers, or pediatric patients because it has not been studied in these patient populations.

**Information for Patients:**

Patients receiving treatment with dronabinol capsules should be advised to inform their prescribing physician if they plan to use alcohol or other CNS depressants because of the potential for additive or synergistic CNS effects.

**Adverse Events:**

Dronabinol 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.

Dronabinol capsules should be used with caution in elderly patients because they have a diminished capacity to cope upon abrupt standing.

Dronabinol capsules are indicated for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

**Usage in Pregnancy and Nursing Mothers:**

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

**Drug Interactions:**

In studies involving patients with AIDS and/or cancer, dronabinol capsules have been co-administered with a variety of medications with beneficial and adverse psychotropic effects.

Dronabinol is highly protein bound to plasma proteins, and therefore, might displace other protein-bound drugs. Although this displacement has not been demonstrated in vivo, clinicians who prescribe dronabinol capsules should monitor patients for a change in dosage requirements.
Contraindications to Dronabinol Use

- Hypersensitivity to any component of the preparation
- Moderate to severe hepatic impairment
- Severe respiratory insufficiency

Warnings

- Dronabinol is a Schedule I substance under the Controlled Substances Act and is listed as such in the Federal Register.
- Pregnancy Category C. Reproduction studies in mice, rats, and rabbits have revealed no evidence of impaired fertility or harm to the fetus produced by dronabinol. However, there are no adequate and well-controlled studies in pregnant women. Dronabinol should be used only in pregnant women when clearly needed.

Adverse Reactions

The most frequently reported adverse experiences in patients with AIDS during placebo-controlled clinical trials involved the CNS and included 317 patients receiving dronabinol and 68 receiving placebo.

- A cannabinoid-related psychosis associated with confusion, hallucinations, anxiety, paranoia, agitation, paranoia, hyperactivity, and agitation.

Overdosage

Signs and symptoms following MILD dronabinol intoxication include dizziness, euphoria, heightened visual awareness, altered time perception, sedation, conjunctival injection, dry mouth and lachrymation, while MODERATE intoxication includes liver enzyme elevation, increased sensitivity to psychoactive effects and of continued use of drugs of abuse, and severe intoxication include decreased motor coordination, lethargy, slurred speech, and convulsions. Signs and symptoms of severe dronabinol intoxication are not well documented. Patients with severe intoxication may experience panic reactions and seizures may occur in patients with existing seizure disorders.

Storage Conditions

Dronabinol Capsules, USP should be packaged in a well-closed container and stored in a cool, dry place (2 to 30°C [36 to 86°F]). Protect from freezing.

How Supplied

NDC 49884-868-02 Bottle of 60 capsules
NDC 49884-867-02 Bottle of 60 capsules
NDC 49884-867-01 Bottle of 100 capsules
NDC 49884-867-05 Bottle of 500 capsules
NDC 49884-869-01 Bottle of 100 capsules
NDC 49884-869-02 Bottle of 25 capsules
NDC 49884-869-05 Bottle of 500 capsules
NDC 49884-869-15 Bottle of 25 capsules
NDC 49884-868-15 Bottle of 25 capsules
NDC 49884-868-01 Bottle of 100 capsules
NDC 49884-868-05 Bottle of 500 capsules
NDC 49884-869-10 Bottle of 25 capsules
NDC 49884-869-05 Bottle of 500 capsules
NDC 49884-869-02 Bottle of 25 capsules
NDC 49884-868-10 Bottle of 100 capsules
NDC 49884-868-05 Bottle of 500 capsules
NDC 49884-868-15 Bottle of 25 capsules
NDC 49884-867-10 Bottle of 100 capsules
NDC 49884-867-01 Bottle of 100 capsules
NDC 49884-867-02 Bottle of 60 capsules
NDC 49884-867-05 Bottle of 500 capsules
NDC 49884-867-04 Bottle of 100 capsules
NDC 49884-869-05 Bottle of 500 capsules
NDC 49884-868-04 Bottle of 100 capsules
NDC 49884-868-10 Bottle of 100 capsules
NDC 49884-868-15 Bottle of 25 capsules
NDC 49884-869-10 Bottle of 25 capsules
NDC 49884-869-01 Bottle of 100 capsules
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