DRONABINOL- dronabinol solution
Wellhouse Pharma, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DRONABINOL ORAL SOLUTION safely and effectively. See full prescribing information for DRONABINOL ORAL SOLUTION.

DRONABINOL Oral Solution, CII
Initial U.S. Approval: 1985

INDICATIONS AND USAGE

Dronabinol oral solution is a cannabinoid indicated in adults for the treatment of:

- anorexia associated with weight loss in patients with AIDS. (1)
- nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. (1)

DOSAGE AND ADMINISTRATION

Administration (2.1):

- Always use the enclosed calibrated oral dosing syringe.
- The calibrated oral syringe measures a maximum dronabinol oral solution dose of 5 mg. If the prescribed dose is greater than 5 mg, the total dose will need to be divided and drawn up in two or more portions using the oral syringe.
- Take dronabinol oral solution with a full glass of water (6 to 8 ounces).
- Dronabinol oral solution can be administered via silicone enteral feeding tubes.

Anorexia Associated with Weight Loss in Adult Patients with AIDS (2.2):

- The recommended starting dosage is 2.1 mg orally twice daily, one hour before lunch and dinner.
- See the full prescribing information for dosage titration to manage adverse reactions and to achieve desired therapeutic effect.

Nausea and Vomiting Associated with Chemotherapy in Adult Patients Who Failed Conventional Antiemetics (2.3):

- The recommended starting dosage is 4.2 mg/m ^{2}, administered 1 to 3 hours prior to chemotherapy, then every 2 to 4 hours after chemotherapy for a total of 4 to 6 doses per day. Administer the first dose on an empty stomach at least 30 minutes prior to eating; subsequent doses can be taken without regard to meals.
- See the full prescribing information for dosage titration to manage adverse reactions and to achieve desired therapeutic effect.

DOSAGE FORMS AND STRENGTHS

Oral Solution: 5 mg/ mL (3)

CONTRAINDICATIONS

- Sensitivity to dronabinol or alcohol. (4)
- History of hypersensitivity reaction to alcohol. (4)
- Patients receiving, or have received, disulfiram- or metronidazole-containing products within the past 14 days. (4, 5.3, 7.1)

WARNINGS AND PRECAUTIONS

- Neuropsychiatric Adverse Reactions: May cause psychiatric and cognitive effects and impair mental and/or physical abilities. Avoid use in patients with a psychiatric history. Monitor for symptoms and avoid concomitant use of drugs with similar effects. Inform patients not to operate motor vehicles or other dangerous machinery until they are reasonably certain that dronabinol oral solution does not affect them adversely. (5.1)
- Hemodynamic Instability: Patients with cardiac disorders may experience hypotension, hypertension, syncope, or tachycardia. Avoid concomitant use of drugs with similar effects and monitor for hemodynamic changes after initiating or increasing the dosage of dronabinol oral solution. (5.2)
- Interaction with Disulfiram and Metronidazole: May cause disulfiram-like reaction. Discontinue products containing disulfiram or metronidazole at least 14 days before and do not administer 7 days after treatment with dronabinol oral solution. (4, 5.3, 7.1)
- Seizures and Seizure-like Activity: Weigh the potential risk versus benefits before prescribing dronabinol oral solution to patients with a history of seizures, including those requiring anti-epileptic medication or with other factors that lower the seizure threshold. Monitor patients and discontinue if seizures occur. (5.4)
- Multiple Substance Abuse: Assess risk for abuse or misuse in patients with a history of substance abuse or dependence, prior to prescribing dronabinol oral solution and monitor for the development of associated behaviors or conditions. (5.5)
- Paradoxical Nausea, Vomiting, or Abdominal Pain: Consider reduction or discontinuation, if worsening of symptoms while on treatment. (5.6)
- Toxicities Related to Propylene Glycol in Preterm Neonates: The safety and effectiveness of dronabinol oral solution have not been established in pediatric patients. Avoid use in preterm neonates in the immediate postnatal period. (5.7)

ADVERSE REACTIONS

Most common adverse reactions (≥3%) are: abdominal pain, dizziness, euphoria, nausea, paranoid reaction, somnolence, thinking abnormal, and vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Wellhouse Pharma, LLC at 1-844-558-8289 or FDA at MedWatch phone number 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

- Inhibitors and Inducers of CYP2C9 and CYP3A4: May alter dronabinol systemic exposure; monitor for dronabinol-related adverse reactions or loss of efficacy. (7.2)
- Highly Protein-Bound Drugs: Potential for displacement of other drugs from plasma proteins; monitor for adverse reactions to concomitant narrow therapeutic index drugs (e.g., warfarin, cyclosporine, or amphotericin B) when initiating or increasing the dosage of dronabinol oral solution. (7.3)

USE IN SPECIFIC POPULATIONS

- Pregnancy: May cause fetal harm. (8.1)
- Lactation: Advise HIV infected women not to breastfeed due to the potential for HIV transmission. (8.2)
- Geriatric Use: Elderly patients may be more sensitive to the neuropsychiatric and postural hypotensive effects. Consider a lower starting dose in elderly patients. (2.2, 2.3, 5.1, 5.2, 8.5)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.
Revised: 1/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Dronabinol oral solution is indicated in adults for the treatment of:

- anorexia associated with weight loss in patients with Acquired Immune Deficiency Syndrome (AIDS).
- nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

Oral Administration

- Always use the enclosed calibrated oral dosing syringe when administering dronabinol oral solution to ensure the dose is measured and administered accurately.
- The calibrated oral syringe measures a maximum dronabinol oral solution dose of 5 mg. If the prescribed dose is greater than 5 mg, the total dose will need to be divided and drawn up in two or more portions using the oral syringe.
- Take each dose of dronabinol oral solution with a full glass of water (6 to 8 ounces).
- For information on dosing dronabinol with regard to meals, *see Dosage and Administration 2.2 and 2.3.*

Administration via Feeding Tube (silicone only, greater than or equal to 14 French)

Dronabinol oral solution can be administered via enteral feeding tubes that are manufactured using silicone, size greater than or equal to 14 French, such as Naso-Gastric (NG), Gastrostomy Tube (G-tube), Percutaneous Endoscopic Gastrostomy tube (PEG-tube) and Gastro-Jejunostomy tube (GJ-tube). Do not use tubes manufactured of polyurethane.

1. Draw up the prescribed dose with the calibrated dosing syringe packaged with

dronabinol oral solution.
2. If the prescribed dose is greater than 5 mg, the total dose will need to be divided and drawn up in two or more portions using the oral syringe.
3. Using the calibrated dosing syringe, administer the dose via the feeding tube.
4. Using a catheter-tip syringe, flush the feeding tube with 30 mL of water.

2.2 Anorexia Associated with Weight Loss in Adult Patients with AIDS

Starting Dosage

The recommended adult starting dosage of dronabinol oral solution is 2.1 mg orally twice daily, one hour before lunch and one hour before dinner.

In elderly patients, or patients unable to tolerate 2.1 mg twice daily, consider initiating dronabinol oral solution at 2.1 mg once daily one hour before dinner or at bedtime to reduce the risk of central nervous system (CNS) symptoms *[see Use in Specific Populations (8.5)]*.

Dosing later in the day may reduce the frequency of Central Nervous System (CNS) adverse reactions. CNS adverse reactions are dose-related *[see Warnings and Precautions (5.1)]*; therefore, monitor patients and reduce the dosage as needed. If CNS adverse reactions of feeling high, dizziness, confusion, and somnolence occur, they usually resolve in 1 to 3 days and usually do not require dosage reduction. If CNS adverse reactions are severe or persistent, reduce the dosage to 2.1 mg once daily one hour before dinner or in the evening at bedtime.

Dosage Titration
- If tolerated and further therapeutic effect is desired, the dosage may be increased gradually to 2.1 mg one hour before lunch and 4.2 mg one hour before dinner. Increase the dose of dronabinol oral solution gradually in order to reduce the frequency of dose-related adverse reactions *[see Warnings and Precautions (5.1)]*.
- Most patients respond to 2.1 mg twice daily, but the dose may be further increased to 4.2 mg one hour before lunch and 4.2 mg one hour before dinner, as tolerated to achieve a therapeutic effect.
- Maximum Dosage: 8.4 mg twice daily.

2.3 Nausea and Vomiting Associated with Cancer Chemotherapy in Adult Patients Who Failed Conventional Antiemetics

Starting Dosage

The recommended starting dosage of dronabinol oral solution is 4.2 mg/m^2 orally administered 1 to 3 hours prior to chemotherapy and then every 2 to 4 hours after chemotherapy for a total of 4 to 6 doses per day.
- Calculate the starting dose by following the steps below:
  - Starting dose (mg) = Patient body surface area (BSA) in m^2 multiplied by 4.2 mg/m^2
  - Round dose to the nearest 0.1 mg increment
  - Convert from milligrams (mg) to milliliters (mL):
    - Starting dose (mg) rounded to the nearest 0.1 mg increment divided by 5 = Starting dose in milliliters (mL)
  - To correspond with the calibrated oral dosing syringe, the dose may need to be rounded to the nearest 0.1 mL increment.

In elderly patients, consider initiating dronabinol oral solution at 2.1 mg/m^2 once daily 1 to 3 hours prior to chemotherapy to reduce the risk of CNS symptoms *[see Use in Specific Populations (8.5)]*.

Because food delays the absorption of dronabinol oral solution, administer the first dose on an empty stomach at least 30 minutes before eating. Subsequent doses can be taken without regard to meals.

Because food can substantially change the systemic exposure to dronabinol and its active metabolite, the timing of dosing in relation to meal times should be kept consistent for each chemotherapy cycle, once the dosage has been determined from the titration process.

Dosage Titration
- The dosage can be titrated to clinical response during a chemotherapy cycle or subsequent cycles, based upon initial effect, as tolerated to achieve a clinical effect, in increments of 2.1 mg/m^2.
- Maximum Dosage: 12.6 mg/m^2 per dose for 4 to 6 doses per day.
- Adverse reactions are dose-related and psychiatric symptoms increase significantly at the maximum dosage *[see Warnings and Precautions (5.1)]*.

Monitor patients for adverse reactions and consider decreasing the dose to 2.1 mg once daily 1 to 3 hours prior to chemotherapy to reduce the risk of CNS adverse reactions.

3 DOSAGE FORMS AND STRENGTHS

Oral Solution: 5 mg/mL, a clear, pale yellow to brown solution.

4 CONTRAINDICATIONS

Dronabinol oral solution is contraindicated in patients:
- with a history of a hypersensitivity reaction to dronabinol. Reported hypersensitivity reactions to dronabinol include lip swelling, hives, disseminated rash, oral lesions, skin burning, flushing, throat tightness *[see Adverse Reactions (6.2)]*.

- with a history of a hypersensitivity reaction to alcohol.
- who are receiving, or have recently received, disulfiram- or metronidazole-containing products within 14 days *[see Warning and Precautions (5.3)]*. Dronabinol oral solution contains 50% (w/w) dehydrated alcohol and 5.5% (w/w) propylene glycol.

5 WARNINGS AND PRECAUTIONS

5.1 Neuropsychiatric Adverse Reactions

Psychiatric Adverse Reactions

Dronabinol has been reported to exacerbate mania, depression, or schizophrenia. Prior to initiating treatment with dronabinol oral solution, screen patients for a history of these illnesses. Avoid use in patients with a psychiatric history or, if the drug cannot be avoided, monitor patients for new or worsening psychiatric symptoms during treatment. Also, avoid concomitant use with other drugs that are associated with similar psychiatric effects.

Cognitive Adverse Reactions

Use of dronabinol oral solution has been associated with cognitive impairment and altered mental state. Reduce the dose of dronabinol oral solution or discontinue use of dronabinol oral solution if signs or symptoms of cognitive impairment develop. Elderly and pediatric patients may be more sensitive to the neurological and psychoactive effects of dronabinol oral solution *[see Use in Specific Populations (8.4, 8.5)]*.

Hazardous Activities

Dronabinol oral solution can cause and may impair the mental and/or physical abilities required for the performance of hazardous tasks such as driving a motor vehicle or operating machinery. Concomitant use of other drugs that cause dizziness, confusion, sedation, or somnolence such as CNS depressants may increase this effect (e.g., barbiturates, benzodiazepines, lithium, opioids, buspirone, scopolamine, antihistamines, tricyclic antidepressants, other anticholinergic agents, and muscle relaxants). Inform patients not to operate motor vehicles or other dangerous machinery until they are reasonably certain that dronabinol oral solution does not affect them adversely.

5.2 Hemodynamic Instability

Patients may experience occasional hypotension, possible hypertension, syncope, or tachycardia while taking dronabinol oral solution *[see Clinical Pharmacology (12.2)]*. Patients with cardiac disorders may be at higher risk. Avoid concomitant use of other drugs that are also associated with similar cardiac effects (e.g., amphetamines, other sympathomimetic agents, atropine, amoxapine, scopolamine, antihistamines, other anticholinergic agents, amitriptyline, desipramine, other tricyclic antidepressants). Monitor patients for changes in blood pressure, heart rate, and syncope after initiating or increasing the dosage of dronabinol oral solution.

5.3 Interaction with Disulfiram and Metronidazole

Dronabinol oral solution contains 50% (w/w) dehydrated alcohol and 5.5% (w/w) propylene glycol. Use of dronabinol oral solution may cause a disulfiram-like reaction, characterized by abdominal cramps, nausea, vomiting, headaches, and flushing, in patients receiving disulfiram or other drugs that produce this reaction (e.g., metronidazole). Discontinue products containing disulfiram or metronidazole at least 14 days before starting treatment with dronabinol oral solution and do not administer these products within 7 days of completing treatment with dronabinol oral solution *[see Contraindications (4), Drug Interactions (7.3)]*.

When administered concomitantly with propylene glycol, ethanol competitively inhibits the metabolism of propylene glycol, which may lead to elevated concentrations of propylene glycol. However, the contribution of propylene glycol, if any, to the interaction between disulfiram and dronabinol oral solution is unknown.

5.4 Seizures

Seizures and seizure-like activity have been reported in patients receiving dronabinol.

Weigh this potential risk against the benefits before prescribing dronabinol oral solution to patients with a history of seizures, including those receiving anti-epileptic medication or with other factors that can lower the seizure threshold. Monitor patients with a history of seizure disorders for worsened seizure control during dronabinol oral solution therapy.

If a seizure occurs, advise patients to discontinue dronabinol oral solution and contact a healthcare provider immediately.

5.5 Multiple Substance Abuse

Patients with a history of substance abuse or dependence, including marijuana or alcohol, may be more likely to abuse dronabinol oral solution as well. Dronabinol oral solution contains 50% (w/w) dehydrated alcohol.

Assess each patient's risk for abuse or misuse prior to prescribing dronabinol oral solution and monitor patients with a history of substance abuse during treatment with dronabinol oral solution for the development of these behaviors or conditions.

5.6 Paradoxical Nausea, Vomiting, or Abdominal Pain

New or worsening nausea, vomiting, or abdominal pain can occur during treatment with synthetic delta-9 tetrahydrocannabinol (delta-9-THC), the active ingredient in dronabinol

oral solution. In some cases, these adverse reactions were severe (e.g., dehydration, electrolyte abnormalities) and required dose reduction or drug discontinuation. Symptoms are similar to cannabinoid hyperemesis syndrome (CHS), which is described as cyclical events of abdominal pain, nausea, and vomiting in chronic, long-term users of delta-9-THC products.

Because patients may not recognize these symptoms as abnormal, it is important to specifically ask patients or their caregivers about the development or worsening of nausea, vomiting, or abdominal pain while being treated with dronabinol oral solution. Consider dose reduction or discontinuing dronabinol oral solution if a patient develops worsening nausea, vomiting, or abdominal pain while on treatment.

5.7 Toxicity in Preterm Neonates

Dronabinol oral solution contains the excipients dehydrated alcohol (50%, w/w) and propylene glycol (5.5%, w/w). When administered concomitantly with propylene glycol, ethanol competitively inhibits the metabolism of propylene glycol, which may lead to elevated concentrations of propylene glycol. Preterm neonates may be at increased risk of propylene glycol-associated adverse reactions due to a diminished ability to metabolize propylene glycol, thereby, leading to accumulation.

The safety and effectiveness of dronabinol oral solution have not been established in pediatric patients. Avoid dronabinol oral solution in preterm neonates in the immediate postnatal period because of possible propylene glycol-associated toxicities including: hyperosmolarity, with or without lactic acidosis, renal toxicity, CNS depression (including stupor, coma, and apnea), seizures, hypotonia, cardiac arrhythmias, electrocardiogram (ECG) changes, and hemolysis.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The following serious adverse reactions are described below and elsewhere in the labeling.

- Neuropsychiatric Adverse Reactions *[see Warnings and Precautions (5.1)]*
- Hemodynamic Instability *[see Warnings and Precautions (5.2)]*
- Seizures *[see Warnings and Precautions (5.4)]*
- Paradoxical Nausea, Vomiting, and Abdominal Pain *[see Warnings and Precautions (5.6)]*
- Toxicity in Preterm Neonates *[see Warnings and Precautions (5.7)]*

The safety of dronabinol oral solution has been established based on studies of dronabinol capsules. Studies of AIDS-related weight loss included 157 patients receiving dronabinol capsules and 67 receiving placebo. Studies of nausea and vomiting related to cancer chemotherapy included 317 patients receiving dronabinol capsules and 68 receiving placebo. In the tables below is a summary of the adverse reactions in 474 patients exposed to dronabinol capsules in studies.

Studies of different durations were combined by considering the first occurrence of adverse reactions during the first 28 days.

A cannabinoid dose-related “high” (easy laughing, elation and heightened awareness) has been reported by patients receiving dronabinol capsules in both the antiemetic (24%) and the lower dose appetite stimulant clinical trials (8%). 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 dronabinol capsules. About 25% of patients reported a CNS adverse reaction during the first 2 weeks and about 4% reported such a reaction each week for the next 6 weeks thereafter.

Common Adverse Reactions

The following adverse reactions were reported in clinical trials of dronabinol capsules at an incidence greater than 1%.

System Organ Class	**Adverse Reactions**
General	Asthenia
Cardiovascular	Palpitations, tachycardia, vasodilation/facial flush
Gastrointestinal	Abdominal pain*, nausea*, vomiting*
Central Nervous System	Dizziness*, euphoria*, paranoid reaction*, somnolence*, thinking abnormal*, amnesia, anxiety/nervousness, ataxia, confusion, depersonalization, hallucination

*Actual Incidence 3% to 10%

Less Common Adverse Reactions

The following adverse reactions were reported in clinical trials of dronabinol capsules at an incidence less than or equal to 1%.

System Organ Class	**Adverse Reactions**
General	Chills, headache, malaise

Cardiovascular	Hypotension, conjunctival injection *[see Clinical Pharmacology (12.2)]*
Gastrointestinal	Diarrhea, fecal incontinence, anorexia, hepatic enzyme elevation
Musculoskeletal	Myalgias
Central Nervous System	Depression, nightmares, speech difficulties, tinnitus
Respiratory	Cough, rhinitis, sinusitis
Skin	Flushing, sweating
Sensory	Vision difficulties

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of another oral formulation of dronabinol. 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.

General disorders and administration site conditions: fatigue.

Hypersensitivity reactions: lip swelling, hives, disseminated rash, oral lesions, skin burning, flushing, throat tightness *[see Contraindications (4)]*.

Injury, poisoning and procedural complications: fall *[see Use in Specific Populations (8.5)]*.

Nervous system disorders: seizures *[see Warnings and Precautions (5.4)]*, disorientation, movement disorder, loss of consciousness.

Psychiatric disorders: delirium, insomnia, panic attack.

Vascular disorders: syncope *[see Warnings and Precautions (5.2)].*

7 DRUG INTERACTIONS

7.1 Disulfiram and Metronidazole

Dronabinol oral solution contains 50% (w/w) dehydrated alcohol and 5.5% (w/w) propylene glycol, which can produce disulfiram-like reactions when co-administered with disulfiram or other drugs that produce this reaction (e.g., metronidazole). Discontinue products containing disulfiram or metronidazole at least 14 days before starting treatment with dronabinol oral solution and do not administer these products within 7 days of completing treatment with dronabinol oral solution *[see Contraindications (4), Warnings and Precautions (*5.3*)]*.

When administered concomitantly with propylene glycol, ethanol competitively inhibits the metabolism of propylene glycol, which may lead to elevated concentrations of propylene glycol. However, the contribution of propylene glycol, if any, to the interaction between disulfiram and dronabinol oral solution is unknown.

7.2 Effect of Other Drugs on Dronabinol

Dronabinol is primarily metabolized by CYP2C9 and CYP3A4 enzymes. Inhibitors of these enzymes may increase, while inducers may decrease, the systemic exposure of dronabinol and/or its active metabolite resulting in an increase in dronabinol-related adverse reactions or loss of efficacy of dronabinol oral solution.

Monitor for increased dronabinol-related adverse reactions when dronabinol oral solution is co-administered with inhibitors of CYP2C9 (e.g., amiodarone, fluconazole) and inhibitors of CYP3A4 enzymes (e.g., ketoconazole, itraconazole, clarithromycin, ritonavir, erythromycin, grapefruit juice).

7.3 Highly Protein-Bound Drugs

Dronabinol is highly bound to plasma proteins, and therefore, might displace and increase the free fraction of other concomitantly administered protein-bound drugs. Although this displacement has not been confirmed in vivo, monitor patients for increased adverse reactions to narrow therapeutic index drugs (e.g., warfarin, cyclosporine, amphotericin B) when initiating treatment or increasing the dosage of dronabinol oral solution.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Dronabinol oral solution, a synthetic cannabinoid containing alcohol, may cause fetal harm. Avoid use of dronabinol oral solution in pregnant women. Although there is little published data on the use of synthetic cannabinoids during pregnancy, use of cannabis (e.g., marijuana) and use of alcohol during pregnancy have been associated with adverse fetal/neonatal outcomes *(see Clinical Considerations)*. Cannabinoids have been found in the umbilical cord blood from pregnant women who smoke cannabis. In animal reproduction studies, no teratogenicity was reported in mice administered dronabinol (delta-9-THC) at up to 30 times the MRHD (maximum recommended human doses) and up to 5 times the MRHD for patients with AIDS and cancer, respectively. Similar findings were reported in pregnant rats administered dronabinol at up to 5 to 20 times the MRHD and 3 times the MRHD for patients with AIDS and cancer, respectively. Decreased

maternal weight gain and number of viable pups and increased fetal mortality and early resorptions were observed in both species at doses which induced maternal toxicity. In rats, maternal administration of dronabinol from pregnancy (implantation) through weaning was associated with maternal toxicity, including mortality of pups, and adverse developmental and neurodevelopmental effects on the pups at 2 to 20 times the MRHD for patients with AIDS and less than and up to 3.3 times the MRHD for patients with cancer. *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Published studies suggest that during pregnancy, the use of cannabis, which includes THC, whether for recreational or medicinal purposes, may increase the risk of adverse fetal/neonatal outcomes including fetal growth restriction, low birth weight, preterm birth, small-for-gestational age, admission to the neonatal intensive care unit, and stillbirth. Therefore, use of cannabis during pregnancy should be avoided.

Dronabinol oral solution contains alcohol. Published studies have demonstrated that alcohol is associated with fetal harm including central nervous system abnormalities, behavioral disorders, and impaired intellectual development. Avoid use of Dronabinol oral solution in pregnant women.

Data

Human Data

Delta-9-THC has been measured in the cord blood of some infants whose mothers reported prenatal use of cannabis, suggesting that dronabinol may cross the placenta to the fetus during pregnancy. The effects of delta-9-THC on the fetus are not known.

Animal Data

The recommended dose ranges for dronabinol oral solution in patients with AIDS and patients with cancer are designed to achieve the same systemic exposure ranges to delta-9-THC as with the recommended dose ranges for dronabinol capsules. Therefore, animal to human dose multiples, as shown below, are based on the MRHDs (maximum recommended human doses) for dronabinol capsules, instead of the MRHDs for dronabinol oral solution, which are 15% lower. This approach for dose comparison between animals and humans is supported by the demonstrated difference in dronabinol bioavailability between dronabinol oral solution and dronabinol capsules.

Reproduction studies with dronabinol have been performed in mice at 15 to 450 mg/m^2, equivalent to 1 to 30 times the MRHD of 15 mg/m^2/day (dronabinol capsules) in patients with AIDS or 0.2 to 5 times the MRHD of 90 mg/m^2/day (dronabinol capsules) in patients with cancer, and in rats at 74 to 295 mg/m^2 (equivalent to 5 to 20 times the MRHD of 15 mg/m^2/day in patients with AIDS or 0.8 to 3 times the MRHD of 90 mg/m^2/day in patients with cancer). These studies have revealed no evidence of teratogenicity due to delta-9-THC. At these dronabinol dosages in mice and rats, delta-9-THC 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 that produced less maternal toxicity.

Review of published literature indicates that the endocannabinoid system plays a role in neurodevelopmental processes such as neurogenesis, migration, and synaptogenesis. Exposure of pregnant rats to delta-9-THC (during and after organogenesis) may modulate these processes to result in abnormal patterns of neuronal connectivity and subsequent cognitive impairments in the offspring. Nonclinical toxicity studies in pregnant rats and newborn pups have shown prenatal exposure to delta-9-THC that resulted in impairment of motor function, alteration in synaptic activity, and interference in cortical projection of neuron development in the offspring. Prenatal exposure has shown effects on cognitive function such as learning, short- and long-term memory, attention, decreased ability to remember task, and ability to discriminate between novel and same objects. Overall, prenatal exposure to delta-9-THC has resulted in significant and long-term changes in brain development, cognition, and behavior in rat offspring.

In a pre- and post-natal developmental study, female rats administered dronabinol by oral gavage in a vehicle of medium chain triglycerides at doses of 5, 25 and 50 mg/kg/day (equivalent to 1.7, 10, and 20 times the MRHD for patients with AIDS and 0.33, 1.7, and 3.3 times the MRHD for patients with cancer, respectively, based on body surface area) from gestation day 6 (implantation) through lactation day 20 (weaning). Maternal toxicity caused mortality of pups at and above 10 times the MRHD for patients with AIDS and 1.7 times the MRHD for patients with cancer. At 20 times the MRHD for patients with AIDS and 3.3 times the MRHD for patients with cancer, treatment with dronabinol was associated with an increase in the number of dams with 100% pup mortality on lactation days 1 to 4. At 2 and 10 times the MRHD for patients with AIDS and 0.33 and 1.7 times the MRHD for patients with cancer, dronabinol produced adverse effects on the offspring including delays in developmental landmark parameters (e.g., surface righting reflex, negative geotaxis, and air righting reflex), decreased fertility and pregnancy index, reduced ovary and uterus weights, decreased implantations and viable embryos, and increased post-implantation loss.

Neurological adverse effects such as piloerection, landing foot splay and an increase in the number of rears in open field were observed in offspring at 10 and 20 times the MRHD for patients with AIDS and 0.33 and 1.7 times the MRHD for patients with cancer.

Administration of dronabinol in 50% ethanol (used in the vehicle for Dronabinol Oral Solution), was poorly tolerated in maternal animals. Serious adverse signs of toxicity were observed in the control group (vehicle only) and in dronabinol-containing dose groups at 10 and 20 times the MRHD for patients with AIDS and 1.7 and 3.3 times the MRHD for patients with cancer, resulting in termination of all animals at the 50 mg/kg dose level prior to delivery of litters. These animal findings are difficult to interpret due to effects of alcohol in the vehicle.

8.2 Lactation

Risk Summary

For mothers infected with the Human Immunodeficiency Virus (HIV), the Centers for Disease Control and Prevention recommend that HIV-infected mothers not breastfeed their infants to avoid risking postnatal transmission of HIV. Because of the potential for HIV transmission (in HIV-negative infants) and serious adverse reactions in a breastfed infant, instruct mothers not to breastfeed if they are receiving dronabinol oral solution.

For mothers with nausea and vomiting associated with cancer chemotherapy, there are limited data on the presence of dronabinol in human milk, the effects on the breastfed infant, or the effects on milk production. The reported effects of inhaled cannabis transferred to the breastfeeding infant have been inconsistent and insufficient to establish causality. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for dronabinol oral solution and any potential adverse effects on the breastfed infant from dronabinol oral solution or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of dronabinol oral solution have not been established in pediatric patients.

Pediatric patients may be more sensitive to neurological and psychoactive effects of dronabinol oral solution *[see Warnings and Precautions (*5.1*)]*. Dronabinol oral solution contains the excipients 50% (w/w) dehydrated alcohol and 5.5% (w/w) propylene glycol. Ethanol competitively inhibits the metabolism of propylene glycol, which may lead to elevated concentrations of propylene glycol. Preterm neonates may be at increased risk of propylene glycol-associated adverse events due to diminished ability to metabolize propylene glycol, thereby, leading to accumulation *[see Warnings and Precautions (5.7)]*.

8.5 Geriatric Use

Clinical studies of dronabinol capsules in AIDS and cancer patients did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

Elderly patients may be more sensitive to the neuropsychiatric and postural hypotensive effects of dronabinol oral solution *[see Warnings and Precautions (5.1, 5.2)]*.

Elderly patients with dementia are at increased risk for falls as a result of their underlying disease state, which may be exacerbated by the CNS effects of somnolence and dizziness associated with dronabinol oral solution *[see Warnings and Precautions (5.1)]*. These patients should be monitored closely and placed on fall precautions prior to initiating dronabinol oral solution therapy. In antiemetic studies, no difference in efficacy was apparent in patients greater than 55 years of age compared to 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 falls, decreased hepatic, renal, or cardiac function, increased sensitivity to psychoactive effects, and of concomitant disease or other drug therapy *[see Dosage and Administration (2.2, 2.3)]*.

8.6 Effect of CYP2C9 Polymorphism

Published data suggest that systemic clearance of dronabinol may be reduced and concentrations may be increased in presence of CYP2C9 genetic polymorphism. Monitoring for increased adverse reactions is recommended in patients known to carry genetic variants associated with diminished CYP2C9 function *[see Clinical Pharmacology (12.5)]* .

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Dronabinol oral solution contains dronabinol oral solution, a Schedule II controlled substance.

9.2 Abuse

Dronabinol oral solution contains dronabinol, the main psychoactive component in marijuana. Ingestion of high doses of dronabinol increases the risk of psychiatric adverse reactions if abused or misused, while continued administration can lead to addiction. Psychiatric adverse reactions may include psychosis, hallucinations, depersonalization, mood alteration, and paranoia.

In vitro studies demonstrate that dronabinol oral solution can be easily and effectively abused without manipulation. Dronabinol oral solution contains 50% (w/w) dehydrated alcohol *[see Warning and Precautions (*5.5*)]*.

In a randomized, single-dose, double-blind, placebo- and active-controlled crossover pharmacodynamic study of 43 experienced marijuana smokers, "drug liking" responses

and safety of dronabinol oral solution were compared with placebo and dronabinol in sesame oil oral capsules. Treatment arms were 10 mg and 30 mg dronabinol capsules, 10 mg and 30 mg dronabinol from dronabinol oral solution, and placebo oral solution and capsules. Greater “drug liking” scores were reported with the 30 mg dose, compared with the 10 mg dose, for both dronabinol oral solution and dronabinol-containing capsules. Overall, the pharmacodynamic results from this study demonstrated no statistically significant differences in various measures of drug liking for the doses taken, though the dronabinol oral solution results were consistently greater than those of dronabinol capsules. Similarly, observed adverse reactions were greater for dronabinol oral solution. The pharmacodynamic and safety effects of dronabinol oral solution following multiple doses have not been evaluated.

Patients should be instructed to keep dronabinol oral solution in a secure place out of reach of others for whom the medication has not been prescribed.

9.3 Dependence

Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use. Physical dependence manifests by drug class-specific withdrawal symptoms after abrupt discontinuation or a significant dose reduction of a drug. The appearance of a withdrawal syndrome when administration of the drug is terminated is the only actual evidence of physical dependence. Physical dependence can develop during chronic therapy with dronabinol oral solution and develops after chronic abuse of marijuana.

A withdrawal syndrome was reported after the abrupt discontinuation of dronabinol capsules in subjects receiving dosages of 210 mg per day for 12 to 16 consecutive days. Within 12 hours after discontinuation, subjects 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.

10 OVERDOSAGE

Dronabinol oral solution contains 50% (w/w) dehydrated alcohol and 5.5% (w/w) propylene glycol. Ingestion of the product over the recommended dose could result in significant toxicity.

Dronabinol

Signs and symptoms of dronabinol overdose include drowsiness, euphoria, heightened sensory awareness, altered time perception, reddened conjunctiva, dry mouth, tachycardia, memory impairment, depersonalization, mood alteration, urinary retention, reduced bowel motility, decreased motor coordination, lethargy, slurred speech, and postural hypotension. Patients may also experience panic reactions if they have a prior history of nervousness or anxiety and seizures may occur in patients with existing seizure disorders.

It is not known if dronabinol can be removed by dialysis in cases of overdose.

Alcohol

Signs and symptoms of alcohol overdose include changes in mood or behavior, impaired judgment or social functioning and one or more physical signs such as slurred speech, unsteadiness, lack of coordination, increased or irregular heart rate, respiratory depression, impaired attention or loss of consciousness.

Propylene Glycol

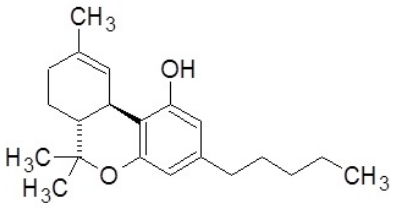
Signs and symptoms of acute poisoning occur only in rare circumstances where patients ingest large amounts of propylene glycol over several days. These include hypoglycemia, severe metabolic acidosis (caused by the metabolism into lactic acid), and CNS depression including coma and seizures.

Management of Overdosage

If over-exposure of dronabinol oral solution occurs, call your Poison Control Center at 1-800-222-1222 for current information on the management of poisoning or overdosage.

11 DESCRIPTION

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



$C_{21}H_{30}O_2$ (molecular weight=314.46)

Dronabinol is a clear colorless to amber oil. Dronabinol is insoluble in water. It has a pKa of 10.6 and an octanol-water partition coefficient: 6,000:1 at pH 7.

Dronabinol oral solution, 5 mg/mL is a clear, pale yellow to brown solution. Each mL of dronabinol oral solution contains 5 mg of dronabinol as an active ingredient and the following inactive ingredients: 50 % (w/w) dehydrated alcohol, polyethylene glycol 400, propylene glycol, sucralose, methyl paraben, propyl paraben, butylated hydroxyanisole, and water.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Dronabinol is an orally active cannabinoid that has complex effects on the 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.

12.2 Pharmacodynamics

Effects on the Cardiovascular System

Dronabinol-induced sympathomimetic activity may result in tachycardia and/or conjunctival injection. Its effects on blood pressure are inconsistent, but subjects have experienced orthostatic hypotension and/or syncope upon abrupt standing *[see Warnings and Precautions (5.2)]*.

Effects on the Central Nervous System

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 inter-patient variability. After oral administration, dronabinol capsules have 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 cardiovascular and CNS pharmacologic effects of dronabinol with chronic use, suggesting an indirect effect on sympathetic neurons. In a study of the pharmacodynamics of chronic dronabinol exposure, healthy male subjects (N = 12) received 12 times the maximum dose for anorexia associated with weight loss in patients with AIDS of dronabinol capsules 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 subjects developed tolerance to the cardiovascular and subjective adverse CNS effects of dronabinol within 12 days of treatment initiation.

Tachyphylaxis and tolerance do not appear to develop to the appetite stimulant effect of dronabinol. In clinical studies of dronabinol capsules in AIDS patients, at the recommended dosage, the appetite stimulant effect was sustained for up to five months.

12.3 Pharmacokinetics

Absorption

Dronabinol (delta-9-THC) is almost completely absorbed (90 to 95%) after a single oral dose. 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. Relative bioavailability data from healthy male and female subjects suggest that a dose of 4.2 mg of dronabinol oral solution provides comparable systemic exposure (C_{max} and AUC) to a 5 mg dronabinol capsule, under fasted conditions *[see Dosage and Administration (2.1)]*. The concentrations of both dronabinol and its major active metabolite (11-hydroxy-delta-9-THC) peak at approximately 0.5 to 4 hours after oral dosing with dronabinol oral solution and decline over several days. The mean inter- and intra-subject variability in dronabinol pharmacokinetics (C_{max} and AUC_{inf}) was approximately 66% and 47% and 67% and 14%, respectively, following administration of dronabinol oral solution to healthy subjects.

Table 1: Summary of Single-Dose Pharmacokinetic Parameters of Dronabinol After Replicated Oral Administration of Dronabinol (4.2 mg to Healthy Subjects under Fasted Conditions)

Parameter*	**Dronabinol**
C_{max} (ng/mL)	1.9 ± 1.3
T_{max} (h)	1.0 [0.5 to 4.0]
$AUC_{(inf)}$ (ng.h/mL)	3.8 ± 1.8
$t_{½}$ (h)	5.6 ± 2.7

* Arithmetic mean ± standard deviation except T_{max} for which the median [range] is reported

Food Effect

The effect of food on the pharmacokinetics of dronabinol oral solution was studied by concomitant dosing of dronabinol oral solution with a high-fat (59 grams of fat, approximately 50% of total caloric content of the meal), high calorie meal (approximately

950 calories). An appreciable food effect was observed: food resulted in approximately a 2.5-fold increase in total exposure (AUC_{inf}) and approximately a 5 hour delay in median T_{max}. Food also decreased C_{max} by approximately 20% *[see Dosage and Administration (2.2, 2.3)]*.

Distribution

Dronabinol has an apparent volume of distribution of approximately 10 L/kg, because of its lipid solubility. The plasma protein binding of dronabinol and its metabolites is approximately 97% *[see Drug Interactions (7.3)]*.

Elimination

The pharmacokinetics of dronabinol can be described using a two compartment model with an initial (alpha) half-life of about 5 hours and a terminal (beta) half-life of 25 to 36 hours. Values for clearance average about 0.2 L/kg-hr; but are highly variable due to the complexity of cannabinoid distribution.

Metabolism

Dronabinol undergoes extensive first-pass hepatic metabolism, primarily by hydroxylation, yielding both active and inactive metabolites. The major metabolite (11-hydroxy-delta-9-THC) is pharmacologically active. Published *in vitro* data indicate that CYP2C9 and CYP3A4 are the primary enzymes in the metabolism of dronabinol. CYP2C9 appears to be the enzyme responsible for the formation of the primary active metabolite *[see Clinical Pharmacology (12.5)]*.

Excretion

Dronabinol and its biotransformation products are excreted in both feces and urine. Biliary excretion is the major route of excretion 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.

Due to its re-distribution, dronabinol and its metabolites may be excreted for prolonged periods of time. Following single dose administration, dronabinol metabolites have been detected for more than 5 weeks in the urine and feces.

In a study of dronabinol 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.

Drug Interaction Studies

Formal drug-drug interaction studies have not been conducted with dronabinol.

The enzyme inhibition and induction potential of dronabinol and its active metabolite are not completely understood.

Published data showed an increase in the elimination half-life of pentobarbital by 4 hours when concomitantly dosed with dronabinol *[see Warnings and Precautions (5.1)]*.

12.5 Pharmacogenomics

Published data indicate a 2- to 3-fold higher dronabinol exposure in individuals carrying genetic variants associated with diminished CYP2C9 function.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The recommended dose ranges for dronabinol oral solution in AIDS and cancer patients are designed to achieve the same systemic exposure ranges as with the recommended dose ranges for dronabinol capsules.

Therefore, the animal to human dose multiples for carcinogenicity studies, as shown below, are based on the MRHD (maximum recommended human dose) for dronabinol capsules in AIDS patients, instead of the MRHD for dronabinol oral solution which is 15% lower. This approach for dose comparison between animals and humans is supported by the demonstrated difference in dronabinol bioavailability between dronabinol oral solution and dronabinol capsules. The animal to human dose multiples for the fertility study in rats, as shown below, are based on the MRHD for dronabinol capsules in AIDS or cancer patients.

In 2-year carcinogenicity studies, there was no evidence of carcinogenicity in rats at doses up to 50 mg/kg/day dronabinol (approximately 20 times the MRHD for dronabinol capsules in AIDS patients on a body surface area basis) or in mice at doses up to 500 mg/kg/day (approximately 100 times the MRHD for dronabinol capsules in AIDS patients on a body surface area basis).

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. However, dronabinol 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 2 to 10 times the MRHD of 15 mg/m^2/day (dronabinol capsules) in AIDS patients or 0.3 to 1.5 times the MRHD of 90 mg/m^2/day (dronabinol capsules) in cancer 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.

14 CLINICAL STUDIES

The effectiveness of dronabinol oral solution has been established based on studies of dronabinol capsules for the treatment of anorexia associated with weight loss in patients with AIDS and nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

16 HOW SUPPLIED/STORAGE AND HANDLING

- Dronabinol oral solution (dronabinol) oral solution, 5 mg/mL is a clear, pale yellow to brown solution. Dronabinol oral solution is supplied in a multi-dose, clear, amber-colored 30 mL glass bottle. It is closed with a 20 mm child-resistant, white polypropylene screw cap with a Teflon coated liner. The bottle is wrapped with a polyvinyl chloride body band to provide tamper evidence and packaged in a carton with an oral syringe, and a push-in bottle adapter.
  NDC 85776-202-30 (30 mL multi-dose bottle, an oral syringe and a push-in bottle adapter)
- Store in a refrigerator between 2°C and 8°C (36°F and 46°F); excursions permitted up to 25°C (77°F). The opened bottle can be stored at 25°C (77°F). Discard unused portion 42 days after first opening [see USP Controlled Room Temperature].
- Keep Dronabinol oral solution and the oral syringe in the supplied carton.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Accidental Ingestion

Inform patients that accidental ingestion of dronabinol oral solution, which contains 50% (w/w) dehydrated alcohol and 5.5% (w/w) propylene glycol, may result in toxicity *[see Overdosage (10)]*. Instruct patients to seek immediate medical attention in case of accidental ingestion. Also, instruct patients to store dronabinol oral solution securely.

Administration Instructions

- Counsel patients on proper dosing and administration techniques. Advise patients to read the Instructions for Use.
- Instruct patients to take each dronabinol oral solution dose with a full glass of water (6 to 8 ounces).

Neuropsychiatric Adverse Reactions*[see Warnings and Precautions (5.1)]*

- Advise patients that psychiatric adverse reactions may occur, especially in patients with a past psychiatric history or in those receiving other drugs also associated with psychiatric effects, and to report to their healthcare provider any new or worsening psychiatric symptoms.
- Advise patients, especially elderly patients, that cognitive impairment or an altered mental state may also occur during treatment with dronabinol oral solution and to report to their healthcare provider if they develop signs or symptoms of cognitive impairment.
- Inform patients not to operate motor vehicles or other dangerous machinery until they are reasonably certain that dronabinol oral solution does not affect them adversely.

Hemodynamic Instability

Advise patients, especially those with cardiac disorders, to report to their healthcare provider if they experience any signs or symptoms of hemodynamic instability, including hypotension, hypertension, syncope or tachycardia, especially after initiating or increasing the dosage of dronabinol oral solution *[see Warnings and Precautions (5.2)]*.

Interaction with Disulfiram and Metronidazole

Inform patients that taking dronabinol oral solution with products containing disulfiram or metronidazole may cause a disulfiram-like reaction due to the alcohol content of dronabinol oral solution. Advise patients not to take products containing disulfiram or metronidazole during treatment with dronabinol oral solution and for up to 7 days of completing treatment with dronabinol oral solution *[see Warnings and Precautions (5.3)]*.

Seizures

Advise patients to discontinue dronabinol oral solution and contact a healthcare provider immediately if they experience a seizure *[see Warnings and Precautions (5.4)].*

Multiple Substance Abuse

Inform patients with a history of substance abuse or dependence, including marijuana or alcohol, that they may be more likely to abuse dronabinol oral solution. Advise patients to report to their healthcare provider if they develop abuse behaviors or conditions *[see Warnings and Precautions (5.5)]*.

Paradoxical Nausea, Vomiting, or Abdominal Pain

Advise patients to report worsening nausea, vomiting, or abdominal pain to their healthcare provider *[see Warnings and Precautions (5.6)]*.

Pregnancy

Advise a pregnant woman of the potential risk to a fetus and to avoid use of dronabinol oral solution during pregnancy. *[see Use in Specific Populations (8.1)].*

Lactation

Advise HIV infected women with anorexia associated with weight loss, not to breastfeed because HIV can be passed to the baby through the breast milk *[see Use in Specific Populations (8.2)].*

Manufactured for:
Wellhouse Pharma, LLC
Round Rock, TX 78665

01/2026

PATIENT INFORMATION
dronabinol oral solution, CII

What is the most important information I should know about dronabinol oral solution?

Dronabinol oral solution can cause serious side effects, including:

- **Worsening mental (psychiatric) symptoms.** Psychiatric symptoms can worsen in people who have mania, depression, or schizophrenia and who take dronabinol oral solution. Dronabinol oral solution taken with medicines that cause psychiatric symptoms can worsen psychiatric symptoms. Elderly people who take dronabinol oral solution may have a greater risk of having psychiatric symptoms. Tell your doctor if you have new or worsening mood symptoms, including symptoms of mania, depression, or schizophrenia.
- **Problems thinking clearly.** Tell your doctor if you have trouble remembering things, concentrating, have increased sleepiness, or confusion. Elderly people may have a greater risk of having problems thinking clearly.
- **Changes in your blood pressure.** Dronabinol oral solution may increase or decrease your blood pressure, especially when you start taking dronabinol oral solution or when your dose is changed. Tell your doctor if you have signs or symptoms of changes in your blood pressure including: headaches, vision problems, dizziness, feeling lightheaded, fainting, or a fast heartbeat. Elderly people, especially those with dementia, and people with heart problems may have an increased risk of changes in blood pressure and an increased risk of falls.
- **Interactions with disulfiram or metronidazole.** Dronabinol oral solution contains alcohol, which can cause you to have a reaction to medicines that contain disulfiram or metronidazole. You should not use any medicine that contains disulfiram (Antabuse) or metronidazole (Pylera, Flagyl, Flagyl ER, Nuvessa, Vandazole) if you take dronabinol oral solution. **You should not use a medicine that contains disulfiram or metronidazole for at least 14 days before you start taking dronabinol oral solution and within 7 days after your last dose of dronabinol oral solution .**Tell your doctor if you have signs or symptoms of a reaction to disulfiram or metronidazole including: stomach-area (abdominal) cramping, nausea, vomiting, headache, and flushing.

What is dronabinol oral solution ?

- **Dronabinol oral solution is a prescription medicine used in adults to treat:**
  - loss of appetite (anorexia) in people with AIDS (Acquired Immune Deficiency Syndrome) who have lost weight.
  - nausea and vomiting caused by anti-cancer medicine (chemotherapy) in people whose nausea and vomiting have not improved with usual anti-nausea medicines.

Dronabinol oral solution is a controlled substance (CII) because it contains dronabinol which can be a target for people who abuse prescription medicines or street drugs. Keep your dronabinol oral solution in a safe place to protect it from theft. Never give your dronabinol oral solution to anyone else because it may cause death or harm them. Selling or giving away this medicine is against the law.
It is not known if dronabinol oral solution is safe and effective in children.

Do not take dronabinol oral solution if you:

- had an allergic reaction to dronabinol. Signs and symptoms of an allergic reaction to dronabinol include: swelling of the lips, hives, a rash over your whole body, mouth sores, skin burning, flushing, and throat tightness.
- had an allergic reaction to alcohol.
- are using a medicine that contains disulfiram (Antabuse) or metronidazole (Pylera, Flagyl, Flagyl ER, Nuvessa, Vandazole) or have taken or received a medicine that contains disulfiram or metronidazole in the last 14 days.

Before taking dronabinol oral solution, tell your doctor about all of your medical conditions, including if you:

- have or had heart problems.
- have or had problems with drug abuse or dependence.
- have or had problems with alcohol abuse or dependence.
- have or had mental health problems including mania, depression or schizophrenia.
- have had a seizure or have a medical condition that may increase your risk of having a seizure.
- are pregnant or plan to become pregnant. Dronabinol oral solution may harm your unborn baby. Avoid the use of dronabinol oral solution if you are pregnant.

- are breastfeeding or plan to breastfeed. The Centers for Disease Control and Prevention recommends that mothers with HIV not breastfeed because they can pass the HIV through their breast milk to the baby. It is not known if dronabinol oral solution passes into your breast milk. Talk to your doctor about the best way to feed your baby if you take dronabinol oral solution.

Tell your doctor about all the medicines you take or have taken in the last 14 days, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Dronabinol oral solution and certain other medicines can affect each other, causing serious side effects.

How should I take dronabinol oral solution?

- See the "Instructions for Use" at the end of the Patient Information for detailed instructions about the right way to take dronabinol oral solution by mouth or through a feeding tube, including the types and sizes of feeding tubes that can be used.
- Always use the oral syringe that comes with your dronabinol oral solution to measure your prescribed dose. Ask your doctor or pharmacist to show you how to measure your prescribed dose.
- Take dronabinol oral solution exactly as your doctor tells you to. Your doctor may change your dose after seeing how it affects you. Do not change your dose unless your doctor tells you to change it.
- If you take dronabinol oral solution by mouth, drink a full glass of water (6 to 8 ounces) right after you take your prescribed dose.
- If you take dronabinol oral solution through a feeding tube, flush the feeding tube with 1 ounce (30 mL) of water using a catheter-tip syringe right after you take your prescribed dose.
- **If you are an adult with AIDS with loss of appetite and weight loss:**
  - Dronabinol oral solution is usually taken 2 times each day, 1 hour before lunch and 1 hour before dinner. If you are elderly, or unable to tolerate this dose of dronabinol oral solution, your doctor may prescribe dronabinol oral solution to be taken 1 time each day, 1 hour before dinner or bedtime.
- **If you are an adult with nausea and vomiting caused by anti-cancer medicine:**
  - Dronabinol oral solution is usually taken 1 to 3 hours before your chemotherapy treatment and then every 2 to 4 hours after chemotherapy for up to 4 to 6 doses each day. If you are elderly, your doctor may prescribe dronabinol oral solution to be taken 1 to 3 hours before your chemotherapy, 1 time each day.
  - Take your first dose of dronabinol oral solution on an empty stomach at least 30 minutes before eating. After your first dose of dronabinol oral solution, you can take dronabinol oral solution with or without food.
  - After your doctor has decided the dose of dronabinol oral solution that is right for you, take dronabinol oral solution exactly at the same time before or after meals during future chemotherapy treatment.
- If you take too much dronabinol oral solution, call your Poison Control Center at 1-800-222-1222 right away or go to the nearest emergency room.

What should I avoid while taking dronabinol oral solution?

- Do not drive, operate machinery, or do other dangerous activities until you know how dronabinol oral solution affects you. Dronabinol oral solution taken with medicines that cause dizziness, confusion, and sleepiness may make these symptoms worse.

What are the possible side effects of dronabinol oral solution?
Dronabinol oral solution may cause serious side effects, including:

- See **"What is the most important information I should know about dronabinol oral solution?"**
- **Seizures.** Dronabinol oral solution may increase your risk of seizures. Stop taking dronabinol oral solution and call your doctor and get medical care right away if you have a seizure during treatment with dronabinol oral solution.
- **Drug and alcohol abuse.** You may have an increased risk of abusing dronabinol oral solution if you have a history of drug or alcohol abuse or dependence, including marijuana. Tell your doctor if you develop abuse behaviors such as increased irritability, nervousness, restlessness or want more or higher doses of dronabinol oral solution during your treatment.
- **Nausea, vomiting, or stomach-area (abdominal) pain.** Tell your doctor if you have nausea, vomiting, or abdominal pain or if your nausea, vomiting, or abdominal pain gets worse during treatment with dronabinol oral solution.

The most common side effects of dronabinol oral solution include:

- stomach-area (abdominal) pain
- dizziness
- feeling extremely happy (euphoria)
- nausea
- overly suspicious or feeling people want to harm you (paranoid reaction)
- sleepiness
- abnormal thoughts
- vomiting

These are not all the possible side effects of dronabinol oral solution. Tell your doctor if you have any side effect that bothers you or does not go away. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of dronabinol oral solution.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use dronabinol oral solution for a condition for which it was

not prescribed. Do not give dronabinol oral solution to other people, even if they have the same symptoms that you have. It may harm them. You can ask your doctor or pharmacist for information about dronabinoloral solution that is written for health professionals.

What are the ingredients in dronabinol oral solution?
Active ingredient: dronabinol
Inactive ingredients: dehydrated alcohol, polyethylene glycol 400, propylene glycol, sucralose, methyl paraben, propyl paraben, butylated hydroxyanisole, and water.

Issued: 01/2026

INSTRUCTIONS FOR USE
Dronabinol
Oral Solution, CII

Read this Instructions for Use before you start taking dronabinol oral solution and each time you get a refill. There may be new information. This information does not take the place of talking to your doctor about your medical condition or your treatment.

Important information about measuring dronabinol oral solution:
- Always use the oral syringe that comes with your dronabinol oral solution to measure your prescribed dose. Ask your doctor or pharmacist to show you how to measure your prescribed dose.

Important information about giving dronabinol oral solution through a feeding tube:
- Give dronabinol oral solution through feeding tubes that are made with silicone and that are size 14 French or larger. **Do not** give dronabinol oral solution through feeding tubes that are not made with silicone or that are smaller than size 14 French.
- **Do not** use feeding tubes made with polyurethane.
- Dronabinol oral solution can be given through a naso-gastric tube (NG tube), gatrostomy tube (G-tube), percutaneous endoscopic gastrostomy tube (PEG-tube), and gastro-jejunostomy tube (GJ-tube).

- Each dronabinol oral solution carton contains (See Figure A):
  - 1 bottle of dronabinol oral solution
  - 1 oral syringe
  - 1 adapter (You will need to insert the adapter into the bottle before using the bottle for the first time.)

  The contents in the dronabinol carton are wrapped in plastic. Do not use the contents if they are not wrapped in plastic when you receive them.

Call Wellhouse Pharma at 1-844-558-8289 if:
- you do not receive an oral syringe or adapter with your dronabinol oral solution
- you lose the oral syringe that comes with dronabinol oral solution
- the contents in the dronabinol oral solution carton are not wrapped in plastic when you receive them.

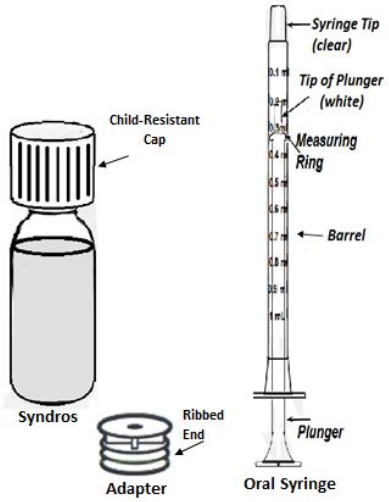


Figure A

How to prepare a bottle of Dronabinol oral solution before using for the first time:

Step 1: Remove the plastic wrap from the bottle and throw it away.

Step 2: Open the bottle by pushing down firmly on the child-resistant cap and turning it counter-clockwise (See Figure B). Do not throw away the child-resistant cap.

Figure B

Step 3: Remove the adapter from the plastic wrap. You may need to use a pair of scissors.

Step 4: Place the open bottle upright on a flat surface. Firmly push down on the adapter until the ribbed end of the adapter fits into the neck of the bottle as far as it will go and is

firmly in place (See Figure C). The top edge of the adapter should be in full contact with the top rim of the bottle. **Do not remove the adapter from the bottle after it is inserted.**

Figure C

Step 5: Follow the instructions in **"How to prepare a dose of dronabinol oral solution after the adapter is inserted."**

How to prepare a dose of dronabinol oral solution after the adapter is inserted:

Step 1: Open the bottle by pushing down firmly on the child-resistant cap and turning it counter-clockwise (See Figure D). Do not throw away the child-resistant cap.

Figure D

Step 2: If you are using the oral syringe for the first time, remove the oral syringe from the plastic wrap. You may need to use a pair of scissors.

Step 3: Hold the oral syringe in one hand. With your other hand, fully push down (depress) the plunger (See Figure E).

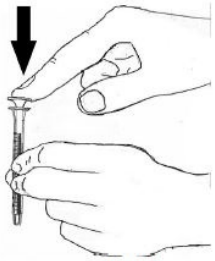


Figure E

Step 4: Keeping the bottle in an upright position, insert the syringe tip firmly into the adapter (See Figure F).

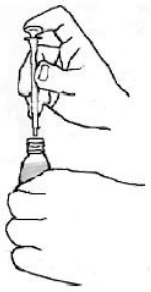


Figure F

Step 5: Carefully turn the bottle upside down with the syringe tip firmly inserted into the adapter (See Figure G).

Figure G

Step 6: Slowly pull back on the plunger until the measuring ring is at the line marking for the dose prescribed by your doctor. The measuring ring is the widest part of the plunger at the bottom of the tip of plunger. (See Figures H(a) and H(b)). Figure H(a) shows a dose of 0.4 mL as an example.

If you see air bubbles in the oral syringe, fully push in the plunger so that the oral solution flows back into the bottle. Then, withdraw your prescribed dose of oral solution.

If your prescribed dose is more than 1 mL, you will need to draw up two or more doses.

For example, if your dose is 1.2 mL, you will need to draw up a 1 mL dose followed by a 0.2 mL dose.

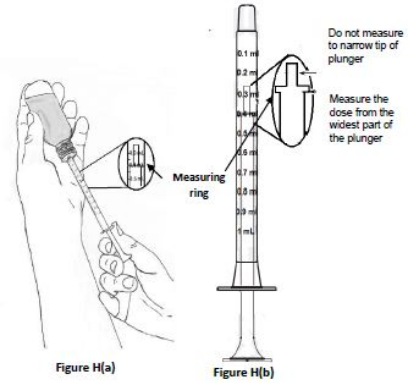


Figure H(a) Figure H(b)

Step 7: Leave the oral syringe in the adapter and turn the bottle to an upright position. Place the bottle onto a flat surface. Remove the oral syringe from the bottle adapter by gently pulling straight up on the oral syringe (See Figure I).

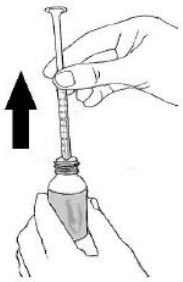


Figure I

Step 8: Check that the correct dose of Dronabinol oral solution was drawn up into the oral syringe.

If the dose is not correct, insert the syringe tip firmly into the bottle adapter. Fully push in the plunger so that the oral solution flows back into the bottle (See Figure J).
Repeat Steps 5-8.
If you are taking your dose of dronabinol oral solution by mouth, follow the instructions in **"How to take a dose of dronabinol oral solution by mouth."**
If you are taking your dose of dronabinol oral solution through a feeding tube, follow the instructions in **"How to take a dose of dronabinol oral solution through a feeding tube."**

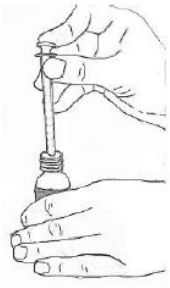


Figure J

How to take a dose of dronabinol oral solution by mouth:

Step 1: Open your mouth. Place the oral syringe tip in the back of your mouth on top of your tongue. Tilt your head back slightly and close your lips around the barrel of the oral syringe. Slowly push down the plunger until the oral syringe is empty (See Figure K).
Swallow the oral solution.
If your prescribed dose is more than 1 mL, repeat Steps 4-8 in **"How to prepare a dose of dronabinol oral solution after the adapter is inserted"** to draw up the remaining dose until the prescribed dose is given. For example, if your prescribed dose is 1.6 mL, take a 1 mL dose first, then an additional dose of 0.6 mL.
Take your dronabinol oral solution right away after it is drawn up into the oral syringe.

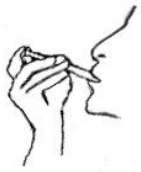


Figure K

Step 2: Drink a full glass of water (6 to 8 ounces) right after you take your prescribed dose of dronabinol oral solution (See Figure L).


Figure L

Step 3: Leave the adapter in the bottle. Put the child-resistant cap back on the bottle (See Figure M).


Figure M

Step 4: Remove the plunger from the oral syringe barrel. Rinse the oral syringe barrel and plunger with warm water after each use and let them air dry. When the oral syringe barrel and plunger are dry, put the plunger back into the oral syringe barrel for the next use. Keep Dronabinol oral solution and the oral syringe in the carton that it comes in. **Do not throw away the oral syringe.**

How to take a dose of dronabinol oral solution through a feeding tube:

See **"Important information about giving dronabinol oral solution through a feeding tube."**
Step 1: Place the oral syringe into the feeding tube. Slowly push down the plunger until the oral syringe is empty (See Figure N).

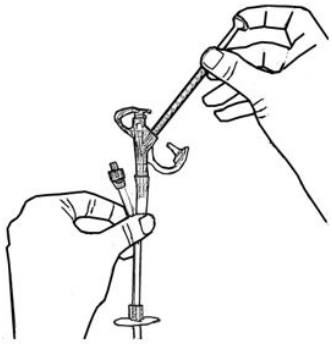


Figure N

If your prescribed dose is more than 1 mL, repeat Steps 4-8 in **"How to prepare a dose of dronabinol oral solution after the adapter is inserted"** to draw up the remaining dose until the prescribed dose is given. For example, if your prescribed dose is 1.6 mL, take a 1 mL dose first, then an additional dose of 0.6 mL.

Take your dronabinol oral solution right away after it is drawn up into the oral syringe.

Step 2: Using a catheter-tip syringe, flush the feeding tube with 1 ounce (30 mL) of water (See Figure O).

Figure O

Step 3: Leave the adapter in the bottle. Put the child-resistant cap back on the bottle (See Figure P).

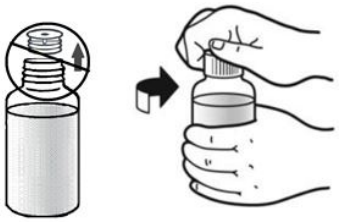


Figure P

Step 4: Remove the plunger from the oral syringe barrel. Rinse the oral syringe barrel and plunger with warm water after each use and let them air dry. When the oral syringe barrel and plunger are dry, put the plunger back into the oral syringe barrel for the next use. Keep Dronabinol oral solution and the oral syringe in the carton that it comes in.

Do not throw away the oral syringe.

How should I store dronabinol oral solution?

- Store dronabinol oral solution in the refrigerator between 36°F and 46°F (2°C and 8°C).
- After the bottle is opened, dronabinol oral solution can be stored at room temperature, between 68°F and 77°F (20°C and 25°C), for up to 42 days.
- Do not use dronabinol oral solution that has been stored in the refrigerator or at room temperature 42 days after opening the bottle. Write the date that you open the bottle of dronabinol oral solution on the bottle and carton it comes in. See **"How should I dispose of unused dronabinol oral solution?"**

Keep dronabinol and all medicines out of the reach of children.

How should I dispose of unused dronabinol oral solution?

- Dispose of unused dronabinol oral solution as soon as you no longer need it or 42 days after opening the bottle.

Talk to your doctor or pharmacist if you have questions about how to use dronabinol oral solution.

For more information, call 1-844-558-8289.

This Patient Information and Instructions for Use have been approved by the U.S. Food

and Drug Administration.

Wellhouse Pharmaceuticals LLC
Round Rock, TX 78665

Revised: January 2026

PRINCIPAL DISPLAY PANEL - NDC: 85776-202-30 - 30 mL Carton Label

NDC 85776-202-30

Dronabinol CII

Oral Solution

5 mg/mL

**Dispense
in original container
with oral syringe
for administration**

Pharmacist: Dispense with Patient Information Leaflet and Instructions for Use provided separately

For oral administration only

**Rx only
30 mL**

Before use: Must be refrigerated, store between 2° and 8° C (36° and 46°F). Once opened, the bottle can be stored at room temperature.

Date of first opening

_____/_____/_____

**Discard unused portion 42 days after opening.
Container includes:**

- 30mL light resistant bottle containing 150mg dronabinol (50mg/mL)
- Oral syringe
- Adapter

Pharmacists: Provide patients with dosing instructions in milliliters (mL) and round dose to nearest 0.1 mL increment.

PROTECT FROM LIGHT.

DO NOT USE IF TAMPER EVIDENT SEAL IS BROKEN OR MISSING.

Dosage: See accompanying package insert for full prescribing information. Each milliliter of dronabinol oral solution contains 5mg dronabinol, 50% w/w dehydrated alcohol, propylene glycol, polyethylene glycol 400, sucralose, methyl paraben, propyl paraben, butylated hydroxyanisole and water. Protect from light by keeping bottle and carton until consumed.

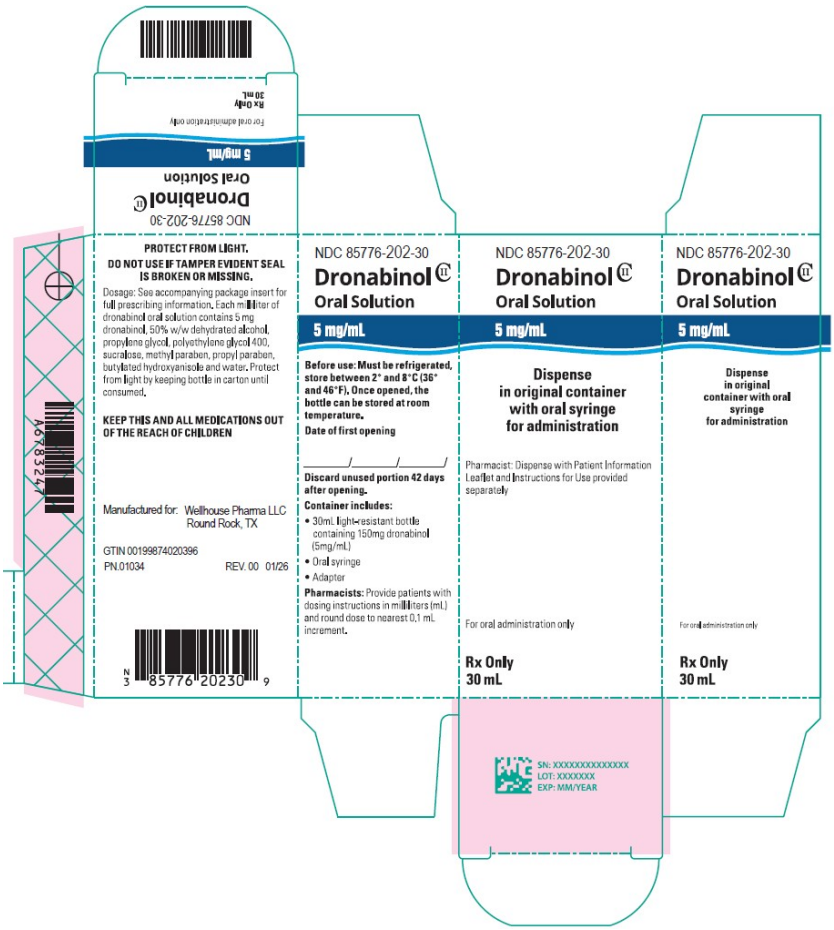
KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN

Manufactured for: Wellhouse Pharma LLC
Round Rock, TX

GTIN 00199874020396
PN.01034 REV. 00 01/26

SN: XXXXXXXXXXXXX
LOT: XXXXXXX

EXP: MM/YEAR



PRINCIPAL DISPLAY PANEL - NDC: 85776-202-30 - 30 mL Bottle Label

NDC 85776-202-30

Dronabinol CII

Oral Solution

5 mg/mL

Dispense in original container with oral syringe for administration

For oral administration only

Rx only
30 mL

Wellhouse

PROTECT FROM LIGHT. DO NOT USE IF TAMPER EVIDENT SEAL IS BROKEN OR MISSING.

Dosage: See accompanying package insert for full prescribing information. Each milliliter of dronabinol oral solution contains 5mg dronabinol, 50% w/w dehydrated alcohol, propylene glycol, polyethylene glycol 400,sucralose, methyl paraben, propyl paraben, butylated hydroxyanisole and water.

Before use: Must be refrigerated, store between 2° and 8° C (36°and 46°F).
Once opened, the bottle can be stored at room temperature.

Date of first opening

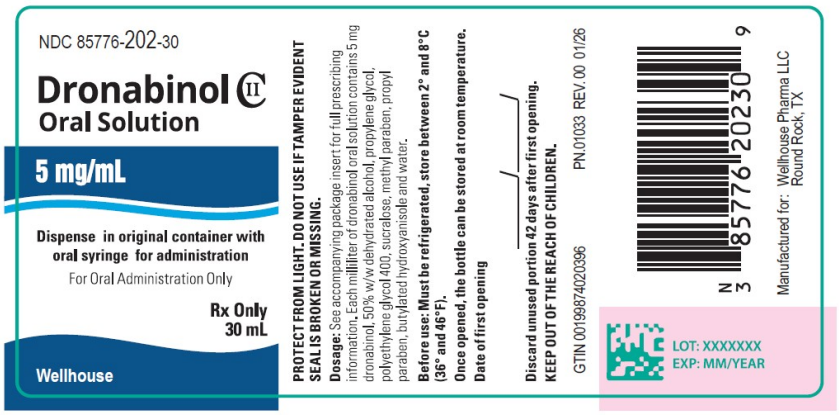
_____/_____/_____

Discard unused portion 42 days after opening.
KEEP OUT OF THE REACH OF CHILDREN

GTIN 00199874020396 PN.01033 REV. 00 01/26

Manufactured for: Wellhouse Pharma LLC
Round Rock, TX

LOT: XXXXXXX
EXP: MM/YEAR



DRONABINOL

dronabinol solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:85776-202
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
DRONABINOL (UNII: 7J8897W37S) (DRONABINOL - UNII:7J8897W37S)	DRONABINOL	5 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:85776-202-30	1 in 1 CARTON	02/11/2026	
1		30 mL in 1 BOTTLE, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA205525	02/11/2026	

Labeler - Wellhouse Pharma, LLC (119521835)

Registrant - Benuvia Operations, LLC (118793457)

Establishment

Name	Address	ID/FEI	Business Operations
Benuvia Operations, LLC		118793457	analysis(85776-202) , api manufacture(85776-202) , label(85776-202) , manufacture(85776-202) , pack(85776-202)

Revised: 2/2026 Wellhouse Pharma, LLC