

Dronabinol

Pronunciation

(droe NAB i nol)

Class

- Antiemetic
- Appetite Stimulant

How Supplied

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Capsule, Oral:

Marinol: 2.5 mg, 5 mg, 10 mg [contains sesame oil]

Generic: 2.5 mg, 5 mg, 10 mg

Action

PHARMACOLOGY:

Unknown, may inhibit endorphins in the brain's emetic center, suppress prostaglandin synthesis, and/or inhibit medullary activity through an unspecified cortical action. Some pharmacologic effects appear to involve sympathimimetic activity; tachyphylaxis to some effect (eg, tachycardia) may occur, but appetite-stimulating effects do not appear to wane over time. Antiemetic activity may be due to effect on cannabinoid receptors (CB1) within the central nervous system.

PHARMACOKINETICS / DYNAMICS:

Absorption:

Oral: 90% to 95%; 10% to 20% of dose gets into systemic circulation

Distribution:

V_d : 10 L/kg; dronabinol is highly lipophilic and distributes to adipose tissue

Metabolism:

Hepatic to at least 50 metabolites, some of which are active; 11-hydroxy-delta-9-tetrahydrocannabinol (11-OH-THC) is the major metabolite; extensive first-pass effect

Excretion:

Feces (35% as unconjugated metabolites, 5% as unchanged drug); urine (10% to 15% as acid metabolites and conjugates)

Onset:

Within 1 hour; Peak effect: 2-4 hours

Peak:

Serum: 0.5-4 hours

Duration:

24 hours (appetite stimulation)

Half-Life elimination:

Dronabinol: 25-36 hours (terminal); Dronabinol metabolites: 44-59 hours

Protein binding:

97% to 99%

Indications

Chemotherapy-associated nausea and vomiting refractory to other antiemetic(s); AIDS-related anorexia

Unlabeled use(s):

Cancer-related anorexia

Contraindications

Hypersensitivity to dronabinol, cannabinoids, sesame oil, or any component of the formulation, or marijuana; should be avoided in patients with a history of schizophrenia

Administration and Dosage

DOSAGE:

Refer to individual protocols. Oral:

Antiemetic: Children and Adults: 5 mg/m² 1-3 hours before chemotherapy, then 5 mg/m²/dose every 2-4 hours after chemotherapy for a total of 4-6 doses/day; increase doses in increments of 2.5 mg/m² to a maximum of 15 mg/m²/dose.

Appetite stimulant: Adults: Initial: 2.5 mg twice daily (before lunch and dinner); titrate up to a maximum of 20 mg/day.

Dosage adjustment in renal impairment: No dosage adjustment provided in manufacturer's labeling.

Dosage adjustment in hepatic impairment: Usual dose should be reduced in patients with severe liver failure.

DIETARY CONSIDERATIONS:

Capsules contain sesame oil.

STORAGE / STABILITY:

Store under refrigeration (or in a cool environment) between 8°C and 15°C (46°F and 59°F); protect from freezing.

Interactions

Alcohol (Ethyl): Dronabinol may enhance the CNS depressant effect of Alcohol (Ethyl). *Monitor therapy*

Anticholinergic Agents: May enhance the tachycardic effect of Cannabinoid-Containing Products. *Monitor therapy*

CNS Depressants: Dronabinol may enhance the CNS depressant effect of CNS Depressants. *Monitor therapy*

Cocaine: May enhance the tachycardic effect of Cannabinoid-Containing Products. *Monitor therapy*

CYP2C9 Inhibitors (Moderate): May increase the serum concentration of Dronabinol. *Monitor therapy*

CYP2C9 Inhibitors (Strong): May increase the serum concentration of Dronabinol. *Monitor therapy*

CYP3A4 Inducers (Strong): May decrease the serum concentration of Dronabinol. *Monitor therapy*

CYP3A4 Inhibitors (Moderate): May increase the serum concentration of Dronabinol. *Monitor therapy*

CYP3A4 Inhibitors (Strong): May increase the serum concentration of Dronabinol. *Monitor therapy*

MAO Inhibitors: May enhance the orthostatic hypotensive effect of Orthostatic Hypotension Producing Agents.

Exceptions: Linezolid; Tedizolid. *Monitor therapy*

Ritonavir: May increase the serum concentration of Dronabinol. *Monitor therapy*

Sympathomimetics: Cannabinoid-Containing Products may enhance the tachycardic effect of Sympathomimetics.
Monitor therapy

Lab Test Interferences:

Decreased FSH, LH, growth hormone, and testosterone

Adverse Reactions

Frequency not always specified.

>1%:

Cardiovascular: Palpitations, tachycardia, vasodilation/facial flushing

Central nervous system: Euphoria (8% to 24%, dose related), abnormal thinking (3% to 10%), dizziness (3% to 10%), paranoia (3% to 10%), somnolence (3% to 10%), amnesia, anxiety, ataxia, confusion, depersonalization, hallucination

Gastrointestinal: Abdominal pain (3% to 10%), nausea (3% to 10%), vomiting (3% to 10%)

Neuromuscular & skeletal: Weakness

<1% (Limited to important or life-threatening): Conjunctivitis, depression, diarrhea, fatigue, fecal incontinence, flushing, hypotension, myalgia, nightmares, seizure, speech difficulties, tinnitus, vision difficulties

Warnings and Precautions

Monitoring:

CNS effects, heart rate, blood pressure, behavioral profile

Pregnancy:

Pregnancy Risk Factor:

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Pregnancy Considerations:

Adverse events have been observed in animal reproduction studies.

Lactation:

Enters breast milk/not recommended

Concerns related to adverse effects:

- CNS depression: May impair physical or mental abilities; patients must be cautioned about performing tasks which require mental alertness (eg, operating machinery or driving).

Disease-related concerns:

- Drug abuse: Use with caution in patients with a history of drug abuse or acute alcoholism; potential for drug dependency exists (drug is psychoactive substance in marijuana). Tolerance, psychological and physical dependence may occur with prolonged use.
- Hepatic impairment: Use with caution in patients with hepatic impairment; reduce dosage with severe impairment.
- Psychiatric disorders: Use with caution in patients with mania, depression, or schizophrenia; careful psychiatric monitoring is recommended.
- Seizure disorder: Use with caution in patients with a history of seizure disorder; may lower seizure threshold.

Concurrent drug therapy issues:

- CNS depressants: Effects may be potentiated when used with other psychoactive drugs, sedatives and/or ethanol.

Special populations:

- Elderly: Use with caution in the elderly; may cause postural hypotension.

Other warnings/precautions:

- Withdrawal: May cause withdrawal symptoms upon abrupt discontinuation.

Patient / Family Education

- Discuss specific use of drug and side effects with patient as it relates to treatment. (HCAHPS: During this hospital stay, were you given any medicine that you had not taken before? Before giving you any new medicine, how often did hospital staff tell you what the medicine was for? How often did hospital staff describe possible side effects in a way you could understand?)
- Patient may experience fatigue, dyspepsia, nausea, or asthenia. Have patient report immediately to prescriber illogical thinking, severe dizziness, syncope, considerable headache, behavioral changes, mood changes, tachycardia, arrhythmia, hallucinations, memory impairment, vision changes, or change in balance (HCAHPS).
- Educate patient about signs of a significant reaction (eg, wheezing; chest tightness; fever; itching; bad cough; blue skin color; seizures; or swelling of face, lips, tongue, or throat). **Note:** This is not a comprehensive list of all side

effects. Patient should consult prescriber for additional questions.

Should not be printed and given to patients. This information is intended to serve as a concise initial reference for healthcare professionals to use when discussing medications with a patient. You must ultimately rely on your own discretion, experience and judgment in diagnosing, treating and advising patients.

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Nabilone

Pronunciation

(NA bi lone)

Class

- Antiemetic

How Supplied

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Capsule, Oral:

Cesamet: 1 mg [contains fd&c blue #2 (indigotine)]

Action

PHARMACOLOGY:

Antiemetic activity may be due to effect on cannabinoid receptors (CB1) within the central nervous system.

PHARMACOKINETICS / DYNAMICS:

Absorption:

Rapid and complete

Distribution:

~12.5 L/kg

Metabolism:

Extensively metabolized to several active metabolites by oxidation and stereospecific enzyme reduction; CYP450 enzymes may also be involved

Excretion:

Feces (~60%); renal (~24%)

Peak:

Serum: Within 2 hours

Half-Life elimination:

Parent compound: ~2 hours; Metabolites: ~35 hours

Special Populations:

Note -

Hepatic and Renal Function Impairment -

Effects have not been determined.

Indications

Treatment of refractory nausea and vomiting associated with cancer chemotherapy

Contraindications

Hypersensitivity to nabilone, other cannabinoids, or any component of the formulation

Administration and Dosage

DOSAGE:

Refer to individual protocols. Oral:

Children >4 years (off-label use; Dupuis, 2003):

<18 kg: 0.5 mg every 12 hours

18-30 kg: 1 mg every 12 hours

>30 kg: 1 mg every 8-12 hours

Adults: 1-2 mg twice daily (maximum: 6 mg divided in 3 doses daily); begin with the lower dose in the range and increase if needed. May administer 2 or 3 times per day during the entire chemotherapy course; continue for up to 48 hours after the last chemotherapy dose. A dose of 1-2 mg the night before chemotherapy may also be of benefit.

Elderly: Refer to adult dosing. Use the lower end of the dosing range (to minimize adverse events).

Dosage adjustment in renal impairment: No dosage adjustment provided in manufacturer's labeling (has not been studied).

Dosage adjustment in hepatic impairment: No dosage adjustment provided in manufacturer's labeling (has not been studied).

ADMINISTRATION:

Initial dose should be given 1-3 hours before chemotherapy.

STORAGE / STABILITY:

Store at 25°C (77°F); excursion permitted to 15°C and 30°C (59°F and 86°F).

Interactions

Alcohol (Ethyl): Nabilone may enhance the CNS depressant effect of Alcohol (Ethyl). *Monitor therapy*

Anticholinergic Agents: May enhance the tachycardic effect of Cannabinoid-Containing Products. *Monitor therapy*

CNS Depressants: Nabilone may enhance the CNS depressant effect of CNS Depressants. *Monitor therapy*

Cocaine: May enhance the tachycardic effect of Cannabinoid-Containing Products. *Monitor therapy*

Sympathomimetics: Cannabinoid-Containing Products may enhance the tachycardic effect of Sympathomimetics.
Monitor therapy

Adverse Reactions

>10%:

Central nervous system: Drowsiness (52% to 66%), dizziness (59%), vertigo (52% to 59%), euphoria (11% to 38%), ataxia (13% to 14%), depression (14%), concentration decreased (12%), sleep disturbance (11%)

Gastrointestinal: Xerostomia (22% to 36%)

Ocular: Visual disturbance (13%)

1% to 10%:

Cardiovascular: Hypotension (8%)

Central nervous system: Dysphoria (9%), headache (6% to 7%), sedation (3%), depersonalization (2%), disorientation (2%)

Gastrointestinal: Anorexia (8%), nausea (4%), appetite increased (2%)

Neuromuscular & skeletal: Weakness (8%)

<1% (Limited to important or life-threatening) and frequency not reported: Abdominal pain, abnormal dreams, akathisia, allergic reaction, amblyopia, anemia, anhydrosis, anxiety, apathy, aphthous ulcer, arrhythmia, back pain, cerebral vascular accident, chest pain, chills, constipation, cough, diaphoresis, diarrhea, dyspepsia, dyspnea, dystonia, emotional disorder, emotional lability, epistaxis, equilibrium dysfunction, eye irritation, fatigue, fever, flushing, gastritis, hallucinations, hot flashes, hyperactivity, hypertension, infection, insomnia, joint pain, leukopenia, lightheadedness, malaise, memory disturbance, mood swings, mouth irritation, muscle pain, nasal congestion, neck pain, nervousness, neurosis (phobic), numbness, orthostatic hypotension, pain, palpitation, panic disorder, paranoia, paresthesia, perception disturbance, pharyngitis, photophobia, photosensitivity, polyuria, pruritus, psychosis (including toxic), pupil dilation, rash, seizure, sinus headache, speech disorder, stupor, syncope, tachycardia, taste perversion, thirst, thought disorder, tinnitus, tremor, urination decreased/increased, urinary retention, visual field defect, voice change, vomiting, wheezing, withdrawal, xerophthalmia

Warnings and Precautions

Monitoring:

Blood pressure, heart rate; signs and symptoms of excessive use, abuse, or misuse

Pregnancy:

Pregnancy Risk Factor:

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Pregnancy Considerations:

Adverse events have been observed in animal reproduction studies.

Lactation:

Excretion in breast milk unknown/not recommended

Concerns related to adverse effects:

- Cardiovascular effects: May cause tachycardia and/or orthostatic hypotension; use with caution in patients

with cardiovascular disease.

- **CNS effects:** May impair physical or mental abilities; patients must be cautioned about performing tasks which require mental alertness (eg, operating machinery or driving). Dizziness, drowsiness, ataxia, depression, hallucinations, and psychosis have been reported. Use with caution in patients with mania, depression, or schizophrenia; cannabinoid use may reveal symptoms of psychiatric disorders. Careful psychiatric monitoring is recommended; psychiatric adverse reactions may persist for up to 3 days after discontinuing treatment.

Disease-related concerns:

- **Substance abuse:** Use with caution in patients with a history of substance abuse; potential for dependency exists. Tolerance, psychological and physical dependence may occur with prolonged use.

Concurrent drug therapy issues:

- **CNS depressants:** Effects may be potentiated when used with other psychoactive drugs, sedatives and/or ethanol.

Special populations:

- **Elderly:** Use with caution in the elderly; may cause postural hypotension.

Patient / Family Education

- Discuss specific use of drug and side effects with patient as it relates to treatment. (HCAHPS: During this hospital stay, were you given any medicine that you had not taken before? Before giving you any new medicine, how often did hospital staff tell you what the medicine was for? How often did hospital staff describe possible side effects in a way you could understand?)
- Patient may experience asthenia, fatigue, xerostomia, or insomnia. Have patient report immediately to prescriber signs of depression (ie, suicidal ideation, anxiety, emotional instability, illogical thinking), severe dizziness, syncope, behavioral changes, mood changes, tachycardia, hallucinations, memory impairment, significant change in balance, or vision changes (HCAHPS).
- Educate patient about signs of a significant reaction (eg, wheezing; chest tightness; fever; itching; bad cough; blue skin color; seizures; or swelling of face, lips, tongue, or throat). **Note:** This is not a comprehensive list of all side effects. Patient should consult prescriber for additional questions.

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