**Brands**
- Marinol, Elevat

**Generic?**
Yes

**Class**
- Cannabinoid agonist; delta-9-tetrahydro-cannabinol (tetrahydrocannabinol [THC])

**Commonly Prescribed For**
(FDA approved in bold)
- Chemotherapy-associated nausea and vomiting refractory to other antiemetic(s)
- AIDS-related anorexia
- Neuropathic pain; especially refractory central neuropathic pain (e.g. multiple sclerosis related pain)
- Cancer pain

**How the Drug Works**
- 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 sympathomimetic activity; tachyphylaxis to some effect (e.g. 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 CNS.

**How Long until It Works**
- May take several weeks to alleviate pain somewhat
- For CNS uses, can take a few weeks to see therapeutic benefits

**If It Works**
- Continue treatment indefinitely and check blood pressure and heart rate regularly
- Continue to monitor effects

**If It Doesn’t Work**
- Consider adjusting dose or switching to another agent with better evidence for CNS efficacy

**Best Augmenting Combos for Partial Response or Treatment-Resistance**
- Best to attempt another monotherapy prior to augmenting for CNS uses

**Tests**
- Blood pressure and heart rate should be checked regularly during treatment

**ADVERSE EFFECTS (AEs)**

**How Drug Causes AEs**
- Excessive actions on cannabinoid (CB) receptors

**Notable AEs**
- Respiratory difficulties, fainting, fatigue, nightmares
- Xerostomia (normal salivary flow resumes upon discontinuation)
- Palpitations, tachycardia, vasodilation/facial flushing, excitability, inability to control thoughts or behavior
- Euphoria, abnormal thinking, dizziness, paranoia, somnolence, amnesia, anxiety, ataxia, confusion, depersonalization, hallucinations, bizarre thought patterns, mood changes, depression
- Abdominal pain, nausea, vomiting
- Muscle weakness, unsteadiness, clumsiness, drowsiness, faintness, psychotic reaction, impaired coordination or judgment

**Life-Threatening or Dangerous AEs**
- Tachycardia, CNS depression
- During withdrawal hypertension

**Weight Gain**
- Unusual
  - Reported but not expected

**Sedation**
- Common
  - Many experience and/or can be significant in amount
  - Some patients may not tolerate it
  - Can abate somewhat with time

**What to Do about AEs**
- Wait
- Take larger dose at bedtime to avoid daytime sedation
- Switch to another medication with better evidence of efficacy
- For withdrawal and discontinuation reactions, may need to reinstate dronabinol and taper very slowly when stabilized
Best Augmenting Agents for AEs
- Dose reduction or switching to another agent may be more effective since most AEs cannot be improved with an augmenting agent

DOSING AND USE

Usual Dosage Range
- 2.5–20 mg/day

Dosage Forms
- Capsule, soft gelatin, oral: 2.5 mg (contains sesame oil), 5 mg (contains sesame oil), 10 mg (contains sesame oil)

How to Dose
- Antiemetic: oral: 5 mg/m² administered 1–3 hours before chemotherapy, then give 5 mg/m² per dose every 2–4 hours after chemotherapy for a total of 4–6 doses/day; dose may be increased up to a maximum of 15 mg/m² per dose if needed (dosage may be increased by 2.5 mg/m² increments)
- Appetite stimulant (AIDS-related): oral: initial 2.5 mg twice daily (before lunch and dinner); titrate up to a maximum of 20 mg/day

Dosing Tips
- Use caution when titrating slow gradual dose increases by 2.5 mg/m²

Overdose
- Hypotension, hypertension, respiratory difficulties, seizures, sedation, weakness, irritability, dysrhythmia

Long-Term Use
- Patients may develop tolerance

Habit Forming
- Reports of some abuse by opioid addicts
- Reports of some abuse by nonopioid-dependent patients

How to Stop
- Discontinuation reactions are common and sometimes severe
- Sudden discontinuation can result in nervousness, agitation, headache, and tremor, with rapid rise in blood pressure
- Taper over 2–4 days or longer to avoid rebound effects (nervousness, increased blood pressure)

Pharmacokinetics
- Onset of action: within 1 hour
- Peak effect: 2–4 hours
- Duration: 24 hours (appetite stimulation)
- Absorption: oral: 90% to 95%; 10% to 20% of dose gets into systemic circulation
- Distribution: Vₚ: 10 L/kg (high); dronabinol is highly lipophilic and distributes to adipose tissue
- Protein binding: 97% to 99%
- 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
- Half-life elimination: Dronabinol 25–36 hours (terminal); Dronabinol metabolites 44–59 hours
- Time to peak, serum: 0.5–4 hours
- Excretion: feces (50% as unconjugated metabolites, 5% as unchanged drug); urine (10% to 15% as acid metabolites and conjugates)

Drug Interactions
- Avoid alcohol (ethyl): CNS depressants may enhance the CNS depressant effect of alcohol
- Anticholinergic agents: may enhance the tachycardic effect of cannabinoids
- CNS depressants: may enhance the adverse/toxic effect of other CNS depressants
- Cocaine: may enhance the tachycardic effect of cannabinoids
- Droperidol: may enhance the CNS depressant effect of cannabinoids. Consider dose reductions of droperidol or of other CNS agents with concomitant use
- Hydroxyzine: may enhance the CNS depressant effect of CNS depressants
- MAOIs: may enhance the orthostatic hypotensive effect of orthostatic hypotension producing agents
- Methotrimeprazine: cannabinoids may enhance the CNS depressant effect of methotrimeprazine. Reduce adult dose of CNS depressant agents by 50% with initiation of concomitant methotrimeprazine therapy
- Ritonavir: may increase the serum concentration of dronabinol
- SSRIs: cannabinoids may enhance the adverse/toxic effect of SSRIs. Specifically, the risk of psychomotor impairment may be enhanced
- Sympathomimetics: cannabinoids may enhance the tachycardic effect of sympathomimetics
- Food: administration with high-lipid meals may increase absorption
- Herb/nutraceutical: St John’s wort may decrease dronabinol levels
**Other Warnings/Precautions**

- May impair physical or mental abilities; patients must be cautioned about performing tasks which require mental alertness (e.g. operating machinery or driving).
- 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.
- Use with caution in patients with mania, depression, or schizophrenia; careful psychiatric monitoring is recommended.
- Use with caution in patients with a history of seizure disorder; may lower seizure threshold.
- CNS depressants: effects may be potentiated when used with other psychoactive drugs, sedatives and/or ethanol.

**Do Not Use**

- If there is a hypersensitivity to dronabinol, cannabinoids, sesame oil, or any component of the formulation, or marijuana; should be avoided in patients with a history of schizophrenia.

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**SPECIAL POPULATIONS**

**Renal Impairment**

- Use with caution and possibly reduce dose.

**Hepatic Impairment**

- Use with caution; reduce dose with severe impairment.

**Elderly**

- Elderly patients may tolerate a lower initial dose better.
- Elderly patients may be more sensitive to the CNS and sedative effects of dronabinol.
- May cause postural hypotension in older adults.
- Older patients may be more sensitive to the CNS effects and postural hypotensive effects of dronabinol. Titrate the dose slowly and monitor for adverse effects.

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**Children and Adolescents**

- Not studied in children.

**Pregnancy**

- Risk Category C.

**Breast-Feeding**

- Some drug is found in mother's breast milk.

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**THE ART OF PAIN PHARMACOLOGY**

**Potential Advantages**

- For CNS indications when conventional treatments have failed (antiemetic, appetite stimulant, analgesic).

**Potential Disadvantages**

- Poor documentation of efficacy for most off-label uses.
- Withdrawal reactions.
- Patients on concomitant CNS medications may have synergistic negative effect on certain neurocognitive functions.
- Miscellaneous AEs with CNS, behavioral, and psychiatric symptoms.

**Primary Target Symptoms**

- Nausea/vomiting.
- Anorexia.
- Pain.

**Pearls**

- Useful as an antiemetic or AIDS-related appetite stimulant.
- Although not approved for pain relief, may be useful in refractory central neuropathic pain (especially refractory pain related to multiple sclerosis) or cancer pain and particularly if associated with anorexia and/or nausea/vomiting.
- May be useful if utilized in conjunction with other agents such as opioids for analgesia.
- In the future, more selective agents may improve efficacy and minimize AEs.
Suggested Reading

