Drug Supply Shortage – Dronabinol

ISSUE

An ongoing national supply disruption is interrupting the dependable availability of products containing **dronabinol** – a cannabinoid with appetite-stimulating and antiemetic properties.

Indications:

- Anorexia Associated with Weight Loss in Adult Patients with AIDS, and
- Nausea and Vomiting Associated with Chemotherapy in Adult Patients Who Failed Conventional Antiemetics.

Dronabinol is a federally controlled substance, scheduled as C-III for capsules and C-II for the solution formulation.

Products include **Marinol®** (dronabinol capsules; 2.5mg), **generic dronabinol capsules** (2.5mg, 5mg, 10mg), and **Syndros®** (dronabinol solution; 5mg/mL). Every product presentation is currently affected by this shortage, as complete product discontinuation by one manufacturer has increased demand and caused shortages of other products across the market.

MANUFACTURER REASON FOR SHORTAGE & PRODUCTS AFFECTED

Major discontinued dronabinol capsules in early-2024.

- Dronabinol oral capsule, Major, 2.5 mg, unit-dose blister pack, 100 count, NDC 00904-7144-61 - discontinued
- Dronabinol oral capsule, Major, 5 mg, unit-dose blister pack, 30 count, NDC 00904-7145-04 – discontinued

Ascend has dronabinol capsules on shortage due to regulatory issues/problems obtaining active ingredient.

- Dronabinol oral capsule, Ascend, 10 mg, bottle, 60 count, NDC 67877-0755-60
- Dronabinol oral capsule, Ascend, 2.5 mg, bottle, 60 count, NDC 67877-0753-60
- Dronabinol oral capsule, Ascend, 5 mg, bottle, 60 count, NDC 67877-0754-60

Rhodes did not provide a reason for the shortage.

- Dronabinol oral capsule, Rhodes, 10 mg, bottle, 60 count, NDC 42858-0869-06
- Dronabinol oral capsule, Rhodes, 2.5 mg, bottle, 60 count, NDC 42858-0867-06
- Dronabinol oral capsule, Rhodes, 5 mg, bottle, 60 count, NDC 42858-0868-06

These product shortages are explicitly detailed on ASHP's Current Drug Shortages webpage. There is no estimated release date provided for any product. Inquires with manufacturers and wholesalers reveal that branded **Marinol capsules** and **Syndros solution** are similarly unavailable/on backorder, with no estimated release date.

ACTION STEPS

PharMerica Pharmacies

- Monitor for product availability and complete orders when possible.
- Promptly notify serviced facilities when prescription orders are unable to be fulfilled due to the drug shortage(s) and provide alternative therapy recommendations as appropriate.

Facilities

- Solicit orders from prescribers for alternative therapies, consistent with residents' indicated conditions, when notified by PharMerica pharmacies of drug shortages.
- Consult with your Consultant Pharmacist as needed for alternative therapy recommendations.

Drug Supply Shortage – Dronabinol

ANOREXIA CLINICAL CONSIDERATIONS

Anorexia is highly prevalent among adult patients with AIDS, leading to unintended weight-loss.

- Depression is a common comorbidity for which residents with involuntary weight loss should be screened.
- Nonpharmacologic interventions should be implemented in adjunct to pharmacologic therapies.
    - Optimize mealtime conditions for resident comfort and satisfaction (comfortable eating environment, food served at proper temperature, etc.).
    - Encourage consumption of favorite foods (regardless of nutritional value).
    - Take into consideration resident-specific factors, such as ethnic food preferences.
    - Consider supplementation with high calorie/ high protein supplements.
- Supportive measures include good mouth care (including denture fit evaluation).

Abridged List of Alternative Therapies (for consideration based on indication for use and resident-specific factors)

- **Megestrol**
    - **Treatment of anorexia, cachexia, or unexplained significant weight loss in patients with AIDS**:
        - Initial (oral): 625 mg daily (of 125 mg/mL suspension) OR 800 mg daily (of 40 mg/mL suspension); daily doses of 400 to 800 mg have been found to be effective.
    - Megestrol is ranked as Acceptable with Caution by the PharMerica P&T committee as it has *not* been shown effective in producing significant weight gain *in the elderly*.
    - Potential side effects include rash, edema, hypogonadism, hyperglycemia, adrenal suppression, and DVT.
        - For the latter reason, megestrol acetate should NOT be used in immobile persons or those with history of thromboembolic disease.
    - According to a retrospective study, megestrol has been associated with an increase in all-cause mortality without increasing weight gain *in elderly nursing home residents*.[1]
    - Current Beers Criteria strongly recommends avoiding megestrol in older adults, due to minimal effect on weight and increased risk of thrombotic events/possibility of death in the elderly.[2]

- **Mirtazapine (Remeron®)**
    - FDA-approval is for major depressive disorder, not anorexia or involuntary weight loss.
    - However, weight gain is a known and common side effect of this antidepressant and it may be a **reasonable option for elderly adults with depression and weight loss**.
        - Onset of significant weight gain has been seen after 1 week of therapy.
    - **Black Box Warning: increased risk of suicidal thoughts and behaviors.**
    - Current Beers Criteria strongly recommends using mirtazapine with caution in older adults, as it may exacerbate or cause SIADH or hyponatremia.[2]

**Summaries provide key clinical information on alternative therapies commonly used for AIDS-related anorexia, and do represent the full prescribing information. Consult the products' package inserts prior to prescribing.*

---

1. Ritchie C, Yukawa M. Geriatric nutrition: Nutritional issues in older adults. UpToDate [subscription required]. https://www.uptodate.com/login. Updated August 9, 2021. Accessed March 5, 2024.
2. American Geriatrics Society 2023 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2023 https://sbgg.org.br/wp-content/uploads/2023/05/1-American-Geriatrics-Society-2023.pdf Updated March 7, 2023. Accessed March 5, 2024.

Drug Supply Shortage – Dronabinol

NAUSEA/VOMITING CLINICAL CONSIDERATIONS

Nausea and vomiting are commonly experienced side effects of chemotherapy. Termed chemotherapy-induced nausea and vomiting (**CINV**), these side effects require effective and readily available antiemetics to help patients manage significant adverse effects on quality of life and their ability to tolerate therapy.

Dronabinol is typically reserved for patients who have failed 'conventional' antiemetics. Facing indefinite unavailability of dronabinol products, prescribers may strategically trial alternative antiemetics to those a patient has failed, choosing therapies with different mechanisms of action.

The article Overview of Chemotherapy-Induced Nausea and Vomiting and Evidence-Based Therapies, published in the American Journal of Managed Care (*Am J Manag Care. 2017;23:S259-S265*) provides a summary of the primary and alternative pharmacologic classes of antiemetics and drug options within these classes (select tables extracted below).

TABLE 3. Antiemetic Agents by Pharmacologic Class[27]

Pharmacologic Class	Agents[a]
5-HT3 receptor antagonists	• Dolasetron mesylate (Anzemet)
	• Granisetron hydrochloride (Granisol, Kytril, Sancuso)
	• Ondansetron base (Zofran ODT, Zuplenz)
	• Ondansetron hydrochloride (Zofran)
	• Palonosetron hydrochloride (Aloxi)
NK1 receptor antagonists	• Aprepitant (Emend)
	• Fosaprepitant dimeglumine (Emend) – prodrug of aprepitant for IV injection
	• Rolapitant (Varubi)
NK1/5-HT3 combination	• Netupitant/palonosetron hydrochloride (Akynzeo)
Corticosteroid	• Dexamethasone (Decadron)
Atypical antipsychotic	• Olanzapine (Zyprexa)
Dopamine antagonists	• Metoclopramide (Reglan)
	• Prochlorperazine (Compazine)
Benzodiazepines	• Alprazolam (Xanax)
	• Lorazepam (Ativan)
Cannabinoids	• Dronabinol (Marinol)
	• Nabilone (Cesamet)

IV: intravenous; ODT: orally disintegrating tablet.
*Agents are listed in alphabetical order within each class and brand names are listed in parentheses where applicable.

TABLE 4. Generalized Antiemetic Guidelines[10,17,22,27,28,59,a]

Chemotherapy Emetic Risk	Recommended Antiemetics[b]
Acute CINV	
High	• NK1 + 5-HT3 + DEX
	• Netupitant/palonosetron + DEX
	• Olanzapine + palonosetron + DEX
	• Aprepitant or fosaprepitant + 5-HT3 + DEX + olanzapine
Moderate	• 5-HT3 + DEX
	• NK1 + 5-HT3 + DEX
	• Netupitant/palonosetron + DEX
	• Olanzapine + palonosetron + DEX
Low	• DEX or DRA or 5-HT3
Minimal	• No routine prophylaxis
Delayed CINV	
High	• Aprepitant + DEX
	• DEX
	• Olanzapine
	• Aprepitant + DEX + olanzapine
Moderate	• DEX
	• 5-HT3 monotherapy
	• Aprepitant +/– DEX
	• DEX
	• Olanzapine
Low	• DEX or DRA or 5-HT3
Minimal	• No routine prophylaxis
Breakthrough/refractory (all risk groups)	Add 1 agent from a different drug class to current regimen, such as:
	• Olanzapine
	• Benzodiazepine
	• Cannabinoid
	• DRA
	• 5-HT3
	• DEX
Anticipatory	• Prevention first
	• Behavioral therapy
	• Acupuncture/acupressure
	• Benzodiazepine

CINV: chemotherapy-induced nausea and vomiting; DEX, dexamethasone; DRA, dopamine receptor antagonist; NK1, neurokinin-1; 5-HT3, 5-HT3 receptor antagonist.
*Order of regimens or agents does not indicate preferential status.
*Specific dosing recommendations can be found in antiemetic guidelines.