BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

SYNDROS™ (dronabinol) oral solution

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Syndros (dronabinol) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Infectious Disease specialist or an Oncologist depending upon indication of use.

  2. Individual is 18 years of age or older.

  3. Individual has a confirmed diagnosis of **ONE** of the following:
     a. Anorexia associated with weight loss in an individual with Acquired Immune Deficiency Syndrome (AIDS) in an individual who is receiving highly active antiretroviral therapy (HAART) (**documentation of weight loss is required**)

b. Nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments

4. The individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. Psychiatric screening for mania, depression, or schizophrenia
   b. Risk assessment for abuse or misuse, especially in those with a history of substance abuse

5. Documented failure, contraindication per FDA label, intolerance, or not a candidate to:
   a. **For anorexia with weight loss due to AIDS, ALL of the following:**
      i. Megestrol acetate
      ii. Marinol (dronabinol) or generic dronabinol cap
   b. **For nausea and vomiting associated with cancer chemotherapy, ALL of the following:**
      i. Cannabinoid, Marinol (dronabinol) or generic dronabinol cap
      ii. Combination of serotonin type 3 receptor antagonist (e.g., granisetron, ondansetron, etc.) plus substance P/neurokinin 1 receptor antagonist (e.g., aprepitant, fosaprepitant, etc.) plus dexamethasone

6. There are **NO** FDA-label contraindications, such as:
   a. History of hypersensitivity reaction to dronabinol
   b. History of hypersensitivity reaction to alcohol
   c. Receiving or have received disulfiram or metronidazole products within the past 14 days

7. Will not be used in a woman who is pregnant or likely to become pregnant

Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Syndros (dronabinol) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Infectious Disease specialist or an Oncologist depending upon indication of use.

2. Individual's condition has responded while on therapy with response defined as **ONE** of the following:
   a. Anorexia associated with weight loss in AIDS syndrome response is defined as **BOTH** of the following:
      i. Achieved and maintains at least a 10% increase in weight **or** has not demonstrated further weight loss
      ii. Continues to receive highly active antiretroviral therapy

   b. Nausea and vomiting associated with cancer chemotherapy response is defined as **BOTH** of the following:
      i. Achieved and maintains at least a 30% improvement in the frequency of nausea and vomiting from cancer chemotherapy (complete or partial response)
      ii. Continues to receive cancer chemotherapy

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Seizure that occurs while on Syndros
        ii. New or worsening nausea, vomiting, or abdominal pain with dehydration and electrolyte abnormalities
        iii. New or worsening psychiatric symptoms such as mania, depression, or schizophrenia
        iv. Hemodynamic instability with hypotension, possible hypertension, syncope, or tachycardia

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Syndros (dronabinol) oral solution is a cannabinoid indicated in adults for the treatment of anorexia associated with weight loss in patients with Acquired Immune Deficiency Syndrome (AIDS); and it is indicated for nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. Syndros (dronabinol) oral solution contains 50% (w/w) dehydrated alcohol and 5.5% (w/w) propylene glycol. It is classified as Schedule II of the Controlled Substances Act.

Dronabinol is synthetic delta-9-tetrahydrocannabinol (delta-9-THC). Delta-9-tetrahydrocannabinol is also a naturally occurring component of *Cannabis sativa L.* (marijuana). Dronabinol has complex effects on the central nervous system, including central sympathomimetic activity. Cannabinoid receptors have been discovered in neural tissues. These receptors may play a role in mediating the effects of dronabinol and other cannabinoids.

Recommendations on treatment of nausea and vomiting due to cancer chemotherapy organize use of medications for nausea and vomiting by the degree of risk for the development of nausea and vomiting from the cancer chemotherapy regimen. For low emetic risk, dexamethasone, metoclopramide, prochlorperazine, or serotonin type 3 receptor antagonists should be used. For moderate emetic risk, a two-drug regimen of dexamethasone plus serotonin type 3 receptor antagonists are recommended. A three-drug regimen of dexamethasone plus serotonin type 3 receptor antagonists plus a substance P/neurokinin is recommended for high emetic risk cancer chemotherapy.

Anorexia, cachexia, and chronic nausea occur frequently in HIV infection. Various treatment options exist for HIV wasting syndrome and include appetite stimulants (megestrol acetate, dronabinol, and mirtazapine) and anabolic agents (testosterone, testosterone analogs). The decision of which agent(s) to choose should include comorbidities, drug–drug interactions, past medical history, and the ability to use and tolerate certain formulations.

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Definitions:

Anti-emetic agents:

Cannabinoid:

1. Cesamet (nabilone) cap
2. Dronabinol cap
3. Marinol (dronabinol) cap
4. Syndros (dronabinol) solution

Serotonin type 3 receptor antagonist:

1. Anzemet (dolasetron) tab
2. Granisetron tab
3. Ondansetron tab, ODT, oral solution
4. Sancuso (granisetron) patch
5. Zuplenz (ondansetron) oral film tab

Substance P/neurokinin 1 (P/NK1) receptor antagonist:

1. Aprepitant cap
2. Emend (aprepitant) cap, oral suspension
3. Varubi (rolapitant) tab

Serotonin type 3 receptor antagonist/ P/NK1 receptor antagonist:

1. Akynzeo (palonosetron/netupitant) cap – requires prior authorization

Other:

1. Dexamethasone
2. Megestrol acetate
3. Metoclopramide
4. Prochlorperazine

Resources:

Syndros (dronabinol) oral solution product information, revised by Insys Therapeutics, Inc. 09-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 01, 2022.

Marinol (dronabinol) capsule product information, revised by ThePharmaNetwork, LLC. 10-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 01, 2022.

Dronabinol capsule product information, revised by Lannett Company, Inc. 04-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 01, 2022.

Bruera E, Dev R. Assessment and management of anorexia and cachexia in palliative care. In: UpToDate, Smith TJ, Given J, Savarese DMF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Topic last updated on November 05, 2021. Available at http://uptodate.com. Accessed August 01, 2022.

Pahuja M, Merlin J, Selwyn PA. Issues in HIV/AIDS in adults in palliative care. In: UpToDate, Morrison RS, Givens J, Bloom A (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on April 26, 2021. Accessed August 01, 2022.

Hesketh PJ. Prevention and treatment of chemotherapy-induced nausea and vomiting in adults. In: UpToDate, Drews RE, Savarese DMF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on January 03, 2022. Accessed August 01, 2022.

Ritchie C, Yukawa M. Geriatric nutrition: Nutritional issues in older adults. In: UpToDate, Schmauder KE, Seres D, Givens J. (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on August 09, 2021. Accessed August 01, 2022.

Badowski ME, Perez SE. Clinical utility of dronabinol in the treatment of weight loss associated with HIV and AIDS. HIV/AIDS research Palliative Care 2016; 8 (Feb 10): 37-45. Re-reviewed August 01, 2022.