BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES		**ORIGINAL EFFECTIVE DATE:**	**7/20/2017**
SECTION:	**DRUGS**	**LAST REVIEW DATE:**	**8/19/2021**
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SYNDROS™ (dronabinol) oral solution

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

SYNDROS™ (dronabinol) oral solution

Criteria:

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

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

2. Individual is 18 years of age or older

3. 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. **ALL** of the following baseline tests have been completed before initiation of treatment:
    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. Individual has failure, contraindication per FDA label, or intolerance 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, **BOTH** of the following:
            1. Cesamet (nabilone) cap
            2. 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

8. There are no significant interacting drugs

Initial approval duration: 12 months

SYNDROS™ (dronabinol) oral solution

- **Criteria for continuation of coverage (renewal request):** Syndros (dronabinol) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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

  2. Individual's condition responded while on therapy is **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. Worsening nausea, vomiting, or abdominal pain while on Syndros

  5. There are no significant interacting drugs

  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 a Non-cancer Medications**

  2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

SYNDROS™ (dronabinol) oral solution

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.

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

SYNDROS™ (dronabinol) oral solution

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:

Dronabinol capsule product information, revised by Ascend Laboratories, LLC. 09-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on August 03, 2021.

Marinaol (dronabinol) capsule product information, revised by ThePharmaNetwork, LLC. 08-2017. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on August 03, 2021.

Syndros (dronabinol) oral solution product information, revised by Benuvia Therapeutics, Inc. 07-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on August 03, 2021.

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. Available at http://uptodate.com. Accessed on August 04, 2021.

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. Accessed on August 04, 2021.

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. Accessed on August 04, 2021.

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 04, 2021.