Clinical Policy: Dronabinol (Marinol, Syndros)

Reference Number: ERX.NPA.74
Effective Date: 09.01.18
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See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Dronabinol (Marinol®, Syndros®) is a cannabinoid.

FDA Approved Indication(s)
Marinol and Syndros are indicated in adults for the treatment of:
- Anorexia associated with weight loss in patients with acquired immune deficiency syndrome (AIDS)
- Nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Marinol and Syndros are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Anorexia Associated with AIDS or Cancer (must meet all)**:**
1. Diagnosis of anorexia with weight loss in patients with AIDS or cancer;
2. Age ≥ 18 years;
3. Prescribed for appetite stimulation;
4. For age < 65 years: Failure of megestrol at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed one of the following (a or b):
   a. Marinol: 20 mg per day (2 capsules per day);
   b. Syndros: 16.8 mg per day.

Approval duration: 6 months

B. Nausea and Vomiting Associated with Cancer Chemotherapy (must meet all)**:**
1. Prescribed for the treatment of chemotherapy-induced nausea/vomiting;
2. Age ≥ 18 years;
3. Member is currently receiving cancer chemotherapy (*see Appendix D*);
4. Failure of a serotonin ($5\text{-}HT_3$) antagonist (*ondansetron or granisetron is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of two of the following at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: metoclopramide, prochlorperazine, lorazepam;
6. Dose does not exceed one of the following (a or b):
   a. Marinol: 15 mg/m^2 per dose (up to 6 doses per day);
   b. Syndros: 12.6 mg/m^2 per dose (up to 6 doses per day).

Approval duration: projected course of chemotherapy up to 72 hours after completion of chemotherapy

C. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member meets one of the following (a or b):
   a. Member has AIDS;
   b. Member continues to receive cancer chemotherapy;
4. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Anorexia associated with AIDS or cancer (i or ii):
      i. Marinol: 20 mg per day (2 capsules per day);
      ii. Syndros: 16.8 mg per day;
   b. Treatment of nausea and vomiting associated with cancer chemotherapy (i or ii):
      i. Marinol: 15 mg/m^2 per dose (up to 6 doses per day);
      ii. Syndros: 12.6 mg/m^2 per dose (up to 6 doses per day).

Approval duration:
Anorexia associated with AIDS or cancer: 12 months
Chemotherapy-induced nausea and vomiting: projected course of chemotherapy up to 72 hours after completion of chemotherapy

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

5-HT$_3$: serotonin 5-hydroxytryptamine, type 3
AIDS: acquired immune deficiency syndrome
ASCO: American Society of Clinical Oncology
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
megestrol (Megace®)	**Anorexia Associated with AIDS** 400 to 800 mg PO QD **Anorexia Associated with Cancer*** 160 to 800 mg PO QD	800 mg/day
5-HT$_3$ Serotonin Antagonists		
Akynzeo® (fosnetupitant/ palonosetron)	**Prevention of nausea and vomiting associated with highly emetogenic chemotherapy** 1 vial IV given 30 min prior to chemotherapy on day 1	1 vial/ chemotherapy cycle
Akynzeo® (netupitant/ palonosetron)	**Prevention of nausea and vomiting associated with highly emetogenic chemotherapy** 1 capsule PO given 1 hour prior to initiation of chemotherapy on day 1 (in combination with	1 capsule or vial/ chemotherapy cycle

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	dexamethasone) or 1 vial IV given 30 min prior to initiation of chemotherapy on day 1	
Aloxi® (palonosetron)	**Prevention of nausea and vomiting associated with chemotherapy** 0.25 mg IV given 30 min prior to chemotherapy	0.25 mg/day
Anzemet® (dolasetron)	**Prevention of nausea and vomiting associated with chemotherapy** 100 mg PO within 1 hr prior to chemotherapy	100 mg/day
granisetron (Kytril®)	**Prevention of nausea and vomiting associated with chemotherapy** Tablet: 2 mg PO QD given 1 hr prior to chemotherapy, or 1 mg PO BID (one dose given 1 hr prior to chemotherapy and then 12 hours later) Injection: 10 mcg/kg IV given within 30 min prior to chemotherapy (on days chemotherapy is given) **Treatment of nausea and vomiting associated with chemotherapy*** 1 to 2 mg PO daily or 1 mg PO BID or 0.01 mg/kg (maximum 1 mg) IV daily	PO: 2 mg/day IV: 10 mcg/kg/day
ondansetron (Zofran®, Zofran® ODT, Zuplenz®)	**Prevention of nausea and vomiting associated with moderately emetogenic chemotherapy** Age 12 years or older: 8 mg PO given 30 min prior to chemotherapy, then repeat dose 8 hrs after initial dose, then 8 mg PO BID for 1 to 2 days after chemotherapy completion Age 4 to 11 years: 4 mg PO given 30 min prior to chemotherapy, then repeat dose 4 and 8 hrs after initial dose, then 8 mg PO TID for 1 to 2 days after chemotherapy completion **Prevention of nausea and vomiting associated with highly emetogenic chemotherapy** 24 mg PO given 30 min prior to start of single-day chemotherapy **Prevention of nausea and vomiting associated with emetogenic chemotherapy** 0.15 mg/kg/dose IV given 30 min prior to chemotherapy, then repeat dose 4 and 8 hrs after initial dose **Treatment of nausea and vomiting associated with chemotherapy*** 16 to 24 mg PO daily or 8 to 16 mg IV	PO: 24 mg/day IV: 16 mg/dose (up to 3 doses/day)
Sancuso® (granisetron)	**Prevention of nausea and vomiting associated with chemotherapy** Apply 1 patch at least 24 hrs prior to chemotherapy; may be applied up to 48 hrs after chemotherapy **Treatment of nausea and vomiting associated with chemotherapy*** Apply 1 patch every 7 days	1 patch/7 days

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Sustol® (granisetron)	**Prevention of moderately emetogenic chemotherapy or anthracycline/cyclophosphamide chemotherapy** 10 mg SC given 30 min prior to chemotherapy on day 1 (in combination with other agents). Do not administer more frequently than once every 7 days.	10 mg/7 days
Miscellaneous Antiemetics		
metoclopramide (Reglan®, Metozolv®)	**Prevention of nausea and vomiting associated with chemotherapy** 1 to 2 mg/kg/dose IV given 30 min prior to chemotherapy. May repeat every 2 hours for 2 doses, then every 3 hours for 3 doses 20 to 40 mg (or 0.5 mg/kg/dose) PO 2 to 4 times daily in combination with dexamethasone*	2 mg/kg/dose (up to 3 doses per day)
lorazepam (Ativan®)	**Prevention of nausea and vomiting associated with chemotherapy*** 0.5 to 2 mg PO, IV, or SL Q6 hrs PRN (in combination with other agents)	10 mg/day
prochlorperazine (Compazine®)	**Prevention of nausea and vomiting associated with chemotherapy*** 10 mg PO/IV once prior to chemotherapy **Treatment of nausea and vomiting** 5 to 10 mg PO 3 to 4 times per day or 25 mg PR BID	Prevention: 10 mg/day Treatment: 40 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications

- Due to risk of disulfiram-like reaction, disulfiram- or metronidazole-containing products should be discontinued 14 days prior to initiating Syndros and should not be administered within 7 days of completing treatment with Syndros.

Appendix D: American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) Recommendations in Oncology

- Minimal emetic risk chemotherapy: No routine prophylaxis is recommended.
- Low emetic risk chemotherapy: Recommended options include dexamethasone (recommended by both ASCO and NCCN) or metoclopramide, prochlorperazine, or a 5-HT_3 receptor antagonist (recommended by NCCN only). NK_1 receptor antagonists are not included in low risk antiemetic recommendations.
- Moderate emetic risk chemotherapy: 5-HT_3 receptor antagonists and dexamethasone may be used in combination and with or without NK_1 receptor antagonists. Olanzapine may also be used in combination with palonosetron and dexamethasone.
  - Examples of moderate emetic risk chemotherapy: azacitidine, alemtuzumab, bendamustine, carboplatin, clofarabine, cyclophosphamide < 1,500 mg/m^2, cytarabine < 1,000 mg/m^2, daunorubicin, doxorubicin, epirubicin, idarubicin, ifosfamide, irinotecan, oxaliplatin
- High emetic risk chemotherapy: NK_1 receptor antagonists are recommended for use in combination with 5-HT_3 receptor antagonists and dexamethasone. Olanzapine may also be used in combination with 5-HT_3 receptor antagonists, dexamethasone, and/or NK_1 receptor antagonists.
  - Examples of high emetic risk chemotherapy: carmustine, cisplatin, cyclophosphamide ≥ 1,500 mg/m^2, dacarbazine, dactinomycin, mechlorethamine, streptozocin

- Breakthrough emesis: Per NCCN, an agent from a different drug class is recommended to be added to the current antiemetic regimen. Drug classes include atypical antipsychotics (olanzapine), benzodiazepines (lorazepam), cannabinoids (dronabinol, nabilone), phenothiazines (prochlorperazine, promethazine), 5-HT_3 receptor antagonists (dolasetron, ondansetron, granisetron), steroids (dexamethasone), or (haloperidol, metoclopramide, scopolamine). An NK_1 receptor antagonist may be added to the prophylaxis regimen of the next chemotherapy cycle if not previously included.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Dronabinol (Marinol)	Anorexia associated with AIDS or cancer	2.5 mg PO BID, may titrate up to 10 mg PO BID	20 mg/day
	Treatment of chemotherapy-induced nausea and vomiting	5 mg/m^2 PO given 1 to 3 hrs prior to chemotherapy, then every 2 to 4 hrs after chemotherapy (total 4 to 6 doses per day). May titrate up to 15 mg/m^2 per dose for 4 to 6 doses per day	15 mg/m^2 per dose (max 6 doses per day)
Dronabinol (Syndros)	Anorexia associated with AIDS or cancer	2.1 mg PO BID, may titrate up to 8.4 mg PO BID	16.8 mg/day
	Treatment of chemotherapy-induced nausea and vomiting	4.2 mg/m^2 PO given 1 to 3 hrs prior to chemotherapy, then every 2 to 4 hrs after chemotherapy (total 4 to 6 doses per day). May titrate up to 12.6 mg/m^2 per dose for 4 to 6 doses per day	12.6 mg/m^2 per dose (max 6 doses per day)

VI. Product Availability

Drug Name	Availability
Dronabinol (Marinol)	Capsules: 2.5 mg, 5 mg, 10 mg
Dronabinol (Syndros)	Oral solution: 5 mg/mL

VII. References

1. Marinol Prescribing Information. North Chicago, IL: AbbVie, Inc; August 2017. Available at http://www.rxabbvie.com/pdf/marinol_PI.pdf. Accessed May 15, 2018.
2. Syndros Prescribing Information. Lakewood, NJ: Insys Therapeutics, Inc.; May 2017. Available at https://www.syndros.com/assets/pdf/SYNDROS-full-prescribing-information.pdf. Accessed May 18, 2018.
3. Hesketh, PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 2017: JCO2017744789.
4. National Comprehensive Cancer Network. Antiemesis Version 1.2018. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed May 15, 2018.
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6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/.
7. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 15, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.15.18	08.18

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.