Clinical Policy: Dronabinol (Marinol, Syndros)

Reference Number: ERX.NPA.74
Effective Date: 09.01.18
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

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. For age < 65 years, one of the following (a or b):
   a. Failure of megestrol at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Request is for Stage IV or metastatic cancer for a State with regulations against step therapy in advanced oncology settings *(see Appendix E*);
4. Dose does not exceed one of the following (a or b):
   a. Marinol: 20 mg (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. Member meets one of the following (a or b):
   a. Both of the following (i and ii):
      i. Failure of a serotonin (5-HT_3) antagonist (*ondansetron and granisetron are preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      ii. Failure of two of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: metoclopramide, prochlorperazine, lorazepam;

b. Request is for Stage IV or metastatic cancer for a State with regulations against step therapy in advanced oncology settings *(see Appendix E*);

5. 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. For nausea and vomiting treatment requests, 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 (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 dexamethasone) or 1 vial IV given 30 min prior to initiation of chemotherapy on day 1	1 capsule or vial/ chemotherapy cycle
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	PO: 24 mg/day IV: 16 mg/dose (up to 3 doses/day)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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/Boxed Warnings

- Contraindication(s):
  - Marinol: history of a hypersensitivity reaction to dronabinol or sesame oil
  - Syndros:
    - History of herpsensitivity reaction to dronabinol or alcohol
    - 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
- Boxed warning(s): none reported

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.

Appendix E: States with Regulations against Redirections in Stage IV or Metastatic Cancer

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial requests only** For stage 4 metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

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 (30 mL bottle)

VII. References

1. Marinol Prescribing Information. North Chicago, IL: AbbVie, Inc; August 2017. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/018651s029lbl.pdf. Accessed October 4, 2021.
2. Syndros Prescribing Information. Lakewood, NJ: Insys Therapeutics, Inc.; July 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/205525Orig1s009lbledt.pdf. . Accessed October 4, 2021.
3. Hesketh, PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Guideline Update. *J Clin Oncol*. 2020. 38:2,782-2,797. doi.org/10.1200/JCO.20.01296.
4. National Comprehensive Cancer Network. Antiemesis Version 1.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed October 1, 2021.
5. National Comprehensive Cancer Network. Palliative Care Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/palliative.pdf. Accessed October 1, 2021.
6. 2019 American Geriatric Society Beers Criteria Update Expert Panel. American Geriatrics Society 2019 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 00:1-21; DOI: 10.1111/jgs.15767.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.15.18	08.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	10.30.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	11.01.19	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	11.12.20	02.21
1Q 2022 annual review: no significant changes; added allowance for bypassing redirection if state regulations do not allow step therapy in Stage IV or metastatic cancer settings with additional details in appendix E; references reviewed and updated.	10.04.21	02.22

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.