Clinical Policy: Dronabinol (Marinol, Syndros)

Reference Number: CP.PMN.159
Effective Date: 11.16.16
Last Review Date: 08.24
Line of Business: Commercial, Medicaid

Coding Implications
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.

It is the policy of health plans affiliated with Centene Corporation® 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 treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
4. Member must use generic dronabinol capsule, unless one of the following (a or b):
   a. Generic dronabinol capsule is contraindicated, or clinically significant adverse effects are experienced;
   b. Request is for Syndros and member is unable to swallow capsules;
5. Dose does not exceed one of the following (a or b):
   a. Marinol: both of the following (i and ii):
      i. 20 mg per day;
      ii. 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 is 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 treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E*);
5. Member must use generic dronabinol capsule, unless one of the following (a or b):
   a. Generic dronabinol capsule is contraindicated, or clinically significant adverse effects are experienced;
   b. Request is for Syndros and member is unable to swallow capsules;
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 (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. For nausea and vomiting treatment requests, member continues to receive cancer chemotherapy;
4. Member must use generic dronabinol capsule, unless one of the following (a or b):
   a. Generic dronabinol capsule is contraindicated, or clinically significant adverse effects are experienced;
   b. Request is for Syndros and member is unable to swallow capsules;
5. 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: both of the following (1 and 2):
         1) 20 mg per day;
         2) 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid, 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 for all relevant lines of business 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)	PO: 2 mg/day IV: 10 mcg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	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	
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)
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 hypersensitivity 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:6zacytidinee, bendamustine, carboplatin, clofarabine, cyclophosphamide ≤ 1,500 mg/m^2, cytarabine > 200 mg/m^2, daunorubicin, doxorubicin < 60 mg/m^2, epirubicin ≤ 90 mg/m^2, 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, 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.

State	Step Therapy Prohibited?	Notes
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.
MS	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
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 and HIM requests only** For stage 4 metastatic cancer and associated conditions
OK	Yes	**Applies to HIM requests only** For advanced 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 hours 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; January 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/018651s033lbl.pdf. Accessed May 9, 2024.
2. Syndros Prescribing Information. Lakewood, NJ: Insys Therapeutics, Inc.; May 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/205525Orig1s013lbl.pdf. Accessed May 21, 2024.
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 1.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed May 2, 2023.
5. National Comprehensive Cancer Network. Palliative Care Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/palliative.pdf. Accessed October 10, 2022.
6. 2023 American Geriatric Society Beers Criteria Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2023; 71: 2052-2081

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
Q0155	Dronabinol (syndros), 0.1 mg, oral, FDA approved prescription antiemetic, for use as a complete therapeutic substitute for an IV antiemetic at the time of chemotherapy treatment, not to exceed a 48 hour dosage regimen.
Q0167	Dronabinol, 2.5 mg, oral, fda approved prescription anti-emetic, for use as a complete therapeutic substitute for an iv anti-emetic at the time of chemotherapy treatment, not to exceed a 48 hour dosage regimen.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; references reviewed and updated.	11.12.20	02.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.	04.27.21	
Added Nevada to Appendix E.	08.03.21	
1Q 2022 annual review: no significant changes; references reviewed and updated.	10.04.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.04.22	
1Q 2023 annual review: added requirement that member must use generic dronabinol capsule, unless contraindicated, clinically significant adverse effects or experienced, or member is unable to swallow capsules; modified to generalize beyond Stage IV or metastatic cancer to the following redirection bypass: "Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings"; references reviewed and updated.	10.10.22	02.23
3Q 2023 annual review: clarified generic redirection bypass if member is unable to swallow capsules applies to Syndros requests only; references reviewed and updated; updated Appendix E to include Oklahoma.	04.19.23	08.23
Added Mississippi to Appendix E.	06.05.24	
3Q 2024 annual review: no significant changes; for anorexia clarified Marinol dose and quantity limits as separate requirements; references reviewed and updated.	05.09.24	08.24
HCPCS codes added [Q0155, Q0167].	11.07.24	

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and

limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.