Clinical Policy Title:	dronabinol
Policy Number:	RxA.225
Drug(s) Applied:	Marinol®, Syndros®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
dronabinol (Marinol®)	Anorexia associated with AIDS or cancer	2.5 mg orally twice a day, may titrate up to 10 mg orally twice a day.	20 mg/day
	Chemotherapy- Induced Nausea and Vomiting (CINV)	5 mg/m^2 orally given 1 to 3 hours prior to chemotherapy, then every 2 to 4 hours afterchemotherapy (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 orally twice a day, may titrate up to 8.4 mg orally twice a day	16.8 mg/day
	Chemotherapy- Induced Nausea and Vomiting (CINV)	4.2 mg/m^2 orally given 1 to 3 hoursprior to chemotherapy, then every 2 to 4 hours 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)

Dosage Forms

- dronabinol (Marinol®): Capsules: 2.5 mg, 5 mg, 10 mg
- dronabinol (Syndros®): Oral solution: 5 mg/mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the term of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 of age or older;
3. For age younger than 65 years: Failure of megestrol at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
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
Commercial: 6 months
Medicaid: 6 months

B. Nausea and vomiting associated with cancer chemotherapy (must meet all)**:**

1. Prescribed for the treatment of CINV;
2. Age 18 years of age or older;
3. Member is currently receiving cancer chemotherapy (*see Appendix D*);
4. Failure of a serotonin (5-HT_3) antagonist at maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of two (2) 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
Commercial: Projected course of chemotherapy up to 72 hours after completion of chemotherapy
Medicaid: Projected course of chemotherapy up to 72 hours after completion of chemotherapy

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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 (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:
Commercial: 12 months
Medicaid: 12 months

CINV:
Commercial: Projected course of chemotherapy up to 72 hours after completion of chemotherapy
Medicaid: Projected course of chemotherapy up to 72 hours after completion of chemotherapy

III. Appendices

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
IV: Intravenous
NCCN: National Comprehensive Cancer Network
CINV: Chemotherapy- Induced Nausea and Vomiting

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
megestrol (Megace®)	Anorexia associated with AIDS: 400 to 800 mg orally daily Anorexia associated with cancer*: 160 to 800 mg daily	800 mg/day
5-HT3 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 per chemotherapy cycle
Akynzeo® (netupitant/ palonosetron)	Prevention of nausea and vomiting associated with highly emetogenic chemotherapy: 1 capsule orally 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 by mouth within 1	100 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	hour prior to chemotherapy	
granisetron (Kytril®)	Prevention of nausea and vomiting associated with chemotherapy: Oral (by mouth): 2 mg orally once a day given 1 hr prior to chemotherapy, or 1 mg orally twice a day (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 orally daily or 1 mg orally twice a day or 0.01 mg/kg (maximum 1 mg) IV daily	By mouth: 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 orally given 30 min prior to chemotherapy, then repeat dose 8 hours after initial dose, then 8 mg orally twice a day for 1 to 2 days after chemotherapy completion Age 4 to 11 years: 4 mg orally given 30 min prior to chemotherapy, then repeat dose 4 and 8 hours after initial dose, then 8 mg orally thrice a day for 1 to 2 days after chemotherapy completion Prevention of nausea and vomiting associated with highly emetogenic chemotherapy 24 mg orally 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 orally daily or 8 to 16 mg IV	By mouth: 24 mg/day IV: 16 mg/dose (up to 3 doses/day)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Sancuso® (granisetron)	Prevention of nausea and vomiting associated with chemotherapy: Apply 1 patch at least 24 hours prior to chemotherapy; may be applied up to 48 hours after chemotherapy Treatment of nausea and vomiting associated with chemotherapy*: Apply 1 patch every 7 days	1 patch per 7 days
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) orally 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 orally, IV, or SL Q6 hours as needed (in combination with other agents)	10 mg/day
prochlorperazine (Compazine®)	Prevention of nausea and vomiting associated with chemotherapy*: 10 mg orally/intravenous once prior to chemotherapy Treatment of nausea and vomiting: 5 to 10 mg orally 3 to 4 times per day or 25 mg PR twice a day	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®:
  - Sensitivity to dronabinol or alcohol;
  - History of hypersensitivity to 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

APPENDIX D: General Information

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 NK1 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.

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy updated: 1. Formatting updated. 2. Clinical title updated 3. Continued criteria for approval updated. 4. Approval duration updated. 5. References updated.	07/28/2020	09/14/2020
Policy updated: 1. Clinical policy Verbiage added "The provision of provider ..." 2. Continued Therapy Approval rephrased to "Member is currently receiving medication.." 3. Appendix A: Abbreviation/Acronym Key added for CINV. 4. Appendix B: Therapeutic Alternatives verbiage updated and abbreviated from PO changed to "By mouth". 5. References were reviewed and updated.	02/25/2021	06/10/2021