RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	**Nabilone**
Policy Number:	RxA.64
Drug(s) Applied:	**Nabilone (Cesamet®)**
Original Policy Date:	01/2020
Last Review Date:	04/2020
Line of Business Policy Applies to:	Commercial

Background

Nabilone (Cesamet®) is a synthetic cannabinoid.

Cesamet is indicated for the treatment of 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
Nabilone (Cesamet®)	Treatment of chemotherapy-induced nausea and vomiting	1 to 2 mg PO BID to TID, starting 1 to 3 hrs prior to chemotherapy and up to 48 hrs after the last dose of each chemotherapy cycle	6 mg/day

Dosage Forms

- Capsules: 1 mg

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.

I. Initial Approval Criteria

A. 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 conventional antiemetic regimens* including monotherapy or combination of NK1 antagonists (eg: aprepitant, fosaprepitant), 5-HT_3 anatgonists (eg: ondansetron, granisetron, dolasetron, palonosetron), or NK-1 anatgonist/5-HT_3 antagonists (eg: netupitant/palonosetron, fosnetupitant/palonosetron) and dexamethasone.

**Some of the preferred agents may need prior authorization*

5. Failure of two of the following at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: olanzapine, metoclopramide, prochlorperazine, lorazepam;
6. Dose does not exceed 6 mg (6 capsules) per day.

Approval Duration: Projected course of chemotherapy up to 72 hours after completion of chemotherapy

II. Continued Therapy Approval

A. Nausea and Vomiting Associated with Cancer Chemotherapy (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Member continues to receive cancer chemotherapy
4. If request is for a dose increase, new dose does not exceed 6 mg (6 capsules) per day.

Approval Duration: Projected course of chemotherapy up to 72 hours after completion of chemotherapy

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

5HT3: serotonin 5-hydroxytryptamine,type 3
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
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/ 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 **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 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)

	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	

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
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		
dexamethasone	**Chemotherapy-induced nausea and vomiting, Prophylaxis** Varies based on emetic risk of chemotherapy drugs and the combination of antiemetics being given	Varies

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
Drug Name	**Dosing Regimen**	**Dose Limit/ Maximum Dose**
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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - History of hypersensitivity to any cannabinoid

- Boxed Warning(s):
  - None reported

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- HT3 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-HT3 receptor antagonists and dexamethasone. Olanzapine may also be used in combination with 5-HT3 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-HT3 receptor antagonists (dolasetron, ondansetron, granisetron), steroids (dexamethasone), or haloperidol, metoclopramide, scopolamine. An NK1 receptor antagonist may be added to the prophylaxis regimen of the next chemotherapy cycle if not previously included.

References

1. Cesamet acrhived drug label. Somerset, NJ: Meda Pharmaceuticals Inc.;September 2018.. Available at: https://dailymed.nlm.nih.gov/dailymed/index.cfm . Accessed April 23, 2020.
2. Hesketh, PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 2017: JCO2017744789
3. National Comprehensive Cancer Network. Antiemesis Version 3.2018. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed October 30, 2018.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/.
5. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed October 30, 2018.
6. Dexamethasone. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI; 2020, March 17. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed April 23, 2020.
7. Olanzapine. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI; 2020, March 17. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed April 23, 2020.
8. Chemotherapy and radiotherapy treatment guidelines for nausea and vomiting. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI; 2020, March 17. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed April 23, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/0/2020
Reviewed criteria - Added trial and failure criteria per ASCO guidelines Updated appendices	04/2020	05/21/2020