Clinical Policy: Nabilone (Cesamet)
Reference Number: ERX.NPA.35
Effective Date: 09.01.17
Last Review Date: 02.19

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Nabilone (Cesamet®) is a synthetic cannabinoid.

FDA Approved Indication(s)
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.

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 Cesamet is medically necessary when the following criteria are met:

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 a serotonin (5-HT3) 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. Failure of dronabinol at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      7. Dose does not exceed 6 mg (6 capsules) per day.
      Approval duration: Projected course of chemotherapy up to 72 hours after completion of chemotherapy

   B. 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. Nausea and Vomiting Associated with Cancer Chemotherapy (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 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
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
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 and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-HT3 Serotonin Antagonists</td>
<td></td>
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</tr>
<tr>
<td>Akynzeo® (fosnetupitant/palonosetron)</td>
<td>Prevention of nausea and vomiting associated with highly emetogenic chemotherapy 1 vial IV given 30 min prior to chemotherapy on day 1</td>
<td>1 vial/chemotherapy cycle</td>
</tr>
<tr>
<td>Akynzeo® (netupitant/palonosetron)</td>
<td>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</td>
<td>1 capsule or vial/chemotherapy cycle</td>
</tr>
<tr>
<td>Aloxi® (palonosetron)</td>
<td>Prevention of nausea and vomiting associated with chemotherapy 0.25 mg IV given 30 min prior to chemotherapy</td>
<td>0.25 mg/day</td>
</tr>
<tr>
<td>Anzemet® (dolasetron)</td>
<td>Prevention of nausea and vomiting associated with chemotherapy 100 mg PO within 1 hr prior to chemotherapy</td>
<td>100 mg/day</td>
</tr>
<tr>
<td>granisetron (Kytril®)</td>
<td>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</td>
<td>PO: 2 mg/day IV: 10 mcg/kg/day</td>
</tr>
<tr>
<td>ondansetron (Zofran®, Zofran® ODT, Zuplenz®)</td>
<td>Prevention of nausea and vomiting associated with moderately emetogenic chemotherapy</td>
<td>PO: 24 mg/day</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/ Maximum Dose</td>
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</tbody>
</table>
| Nabilone             | **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                                                                                                                                                                                                 | 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                                   |
| 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** |                                                                                                                                                                                                                                                                                                                                 |                                                  |
| dronabinol (Marinol®) | Treatment of nausea and vomiting associated with chemotherapy  
5 mg/m² 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/m² per dose for 4 to 6 doses per day.                                                                                                                                                                           | 15 mg/m² per dose (max 6 doses per day)          |
| 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)             |
### Table: Nabilone Dosing Regimens

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>lorazepam (Ativan®)</td>
<td>Prevention of nausea and vomiting associated with chemotherapy*</td>
<td>10 mg/day</td>
</tr>
<tr>
<td></td>
<td>0.5 to 2 mg PO, IV, or SL Q6 hrs PRN (in combination with other agents)</td>
<td></td>
</tr>
<tr>
<td>prochlorperazine (Compazine®)</td>
<td>Prevention of nausea and vomiting associated with chemotherapy*</td>
<td>Prevention: 10 mg/day</td>
</tr>
<tr>
<td></td>
<td>10 mg PO/IV once prior to chemotherapy</td>
<td>Treatment: 40 mg/day</td>
</tr>
<tr>
<td></td>
<td>Treatment of nausea and vomiting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 to 10 mg PO 3 to 4 times per day or 25 mg PR BID</td>
<td></td>
</tr>
</tbody>
</table>

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): history of hypersensitivity to any cannabinoid
- 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-HT3 receptor antagonist (recommended by NCCN only). NK1 receptor antagonists are not included in low risk antiemetic recommendations.
- Moderate emetic risk chemotherapy: 5-HT3 receptor antagonists and dexamethasone may be used in combination and with or without NK1 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/m², cytarabine < 1,000 mg/m², daunorubicin, doxorubicin, epirubicin, idarubicin, ifosfamide, irinotecan, oxaliplatin
- High emetic risk chemotherapy: NK1 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/m², 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.

### V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of chemotherapy-induced nausea and vomiting</td>
<td>1 to 2 mg PO BID to TID, starting 1 to 3 hours prior to chemotherapy and up to 48 hours after the last dose of each chemotherapy cycle</td>
<td>6 mg/day</td>
</tr>
</tbody>
</table>

### VI. Product Availability
Capsules: 1 mg
VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy split from ERX.NSMN.18 Anti-emetics and converted to new template.</td>
<td>07.17.17</td>
<td>08.17</td>
</tr>
<tr>
<td>Removed coverage of Cesamet for radiation-induced nausea/vomiting as this is not an FDA-approved indication, nor is its use for this indication supported by compendia. Added age limit.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3Q 2018 annual review: added requirement that member is receiving cancer chemotherapy for initial and approval criteria; modified trial and failure to a 5-HT3 antagonist (ondansetron or granisetron is preferred); added trial and failure of two other antiemetic agents per NCCN guidelines; revised approval duration to extend to 72 hrs after completion of chemotherapy; references reviewed and updated.</td>
<td>05.15.18</td>
<td>08.18</td>
</tr>
<tr>
<td>1Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>10.30.18</td>
<td>02.19</td>
</tr>
</tbody>
</table>

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.

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