# Clinical Policy: Granisetron (Kytril®, Sancuso®, Sustol®)

Reference Number: PA.CP.PMN.74
Effective Date: 01/18
Last Review Date: 01/19

Coding Implications
Revision Log

**Description**
Granisetron (Kytril®, Sancuso®, Sustol®) is serotonin 5-hydroxytryptamine, type 3 (5-HT3) receptor antagonist.

**FDA approved indication**
Kytril injection is indicated for:

- Prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin
- Prevention and treatment of postoperative nausea and vomiting (PONV) in adults

Kytril tablet is indicated for the prevention of:

- Nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin
- Nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation

Sancuso is indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy of up to 5 consecutive day's duration.

Sustol is indicated in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MED) for anthracycline and cyclcophosphamide (AC) combination chemotherapy regimens.

**Policy/Criteria**
** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria**

It is the policy of Pennsylvania Health and Wellness® that granisetron is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Chemotherapy Induced Nausea and Vomiting** (must meet all)**:**

1. Prescribed for the prevention of chemotherapy-induced nausea and vomiting;
2. Member is scheduled to receive cancer chemotherapy (*see Appendix D*);
3. Failure of a formulary 5-$HT_3$ receptor antagonist (*ondansetron is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
4. For Sancuso and Sustol: medical justification supports inability to use generic granisetron tablet or injection;
5. Request meets one of the following (a, b, c, d, or e):

a. Tablet: Dose does not exceed 2 mg per day;
b. Injection: Dose does not exceed 10 mcg/kg per day;
c. Sustol: Dose does not exceed 10 mg per 7 days;
d. Sancuso: Dose does not exceed 1 patch per 7 days;
e. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

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

**B. Nausea and Vomiting Associated with Radiation Therapy** (must meet all)**:**

1. Request is for granisetron tablet;
2. Prescribed for the prevention of radiation-induced nausea/vomiting;
3. Member is scheduled to receive radiation therapy;
4. Failure of a formulary 5-$HT_3$ receptor antagonist (*ondansetron is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 2 mg per day.

**Approval duration: Projected course of radiation therapy up to 48 hours after completion of radiation therapy**

**C. Postoperative Nausea and Vomiting** (must meet all):

1. Request is for generic granisetron IV injection;
2. Prescribed for the prevention or treatment of postoperative nausea/vomiting;
3. Member is scheduled to undergo surgery;
4. Member meets one of the following (a or b):
   a. For prevention: Failure of a formulary 5-$HT_3$ receptor antagonist (*ondansetron is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. For treatment: Member did not receive a preoperative 5-$HT_3$ receptor antagonist (e.g., ondansetron);
5. Request meets one of the following (a or b):
   a. Dose does not exceed 1 mg once;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 3 days (one time dose)**

**D.** Other diagnoses/indications – Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

## II. Continued Therapy

**A. Postoperative Nausea and Vomiting** (must meet all)**:**
Reauthorization is not permitted. Members must meet the initial approval criteria.

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;

2. Member is responding positively to therapy;
3. Member meets one of the following (a or b):
   a. Member continues to receive cancer chemotherapy (*see Appendix D*);
   b. Member continues to receive radiation therapy;
4. If request is for a dose increase, request meets one of the following (a, b, c, d, or e):
   a. Tablet: New dose does not exceed 2 mg per day;
   b. Injection: New dose does not exceed 10 mcg/kg per day;
   c. Sustol: Dose does not exceed 10 mg per 7 days;
   d. Sancuso: New dose does not exceed 1 patch per 7 days;
   e. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

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

**C. Other diagnoses/indications** (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53 if requested indication is NOT listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

**Approval duration: duration of request or 3 months (whichever is less)**

## 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 policy – PA.CP.PMN.53 or evidence of coverage documents

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

5-$HT_3$: serotonin 5-hydroxytryptamine, type 3
ASCO: American Society of Clinical Oncology
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
PONV: postoperative nausea and vomiting

*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-$HT_3$ Serotonin Antagonists*** | | |
| Akynzeo® (fosnetupitant/ palonosetron) | **Prevention of nausea and vomiting associated with highly emetogenic chemotherapy** | 1 vial/chemotherapy cycle |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| | 1 vial IV given 30 min prior to chemotherapy on day 1 | |
| Akynzeo® (netupitant/ palonosetron) | **Prevention of nausea and vomiting associated with highly emetogenic chemotherapy**<br>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 |
| Anzemet® (dolasetron) | **Prevention of nausea and vomiting associated with chemotherapy**<br>100 mg PO within 1 hr prior to chemotherapy | 100 mg/day |
| Aloxi® (palonosetron) | **Prevention of nausea and vomiting associated with chemotherapy**<br>0.25 mg IV given 30 min prior to chemotherapy<br><br>**Prevention of PONV**<br>0.075 mg IV given immediately prior to anesthesia | Chemo-induced N/V prophylaxis: 0.25 mg/day<br>PONV prophylaxis: 0.075 mg/day |
| ondansetron (Zofran®, Zofran® ODT, Zuplenz®) | **Prevention of nausea and vomiting associated with moderately emetogenic chemotherapy**<br>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<br>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<br><br>**Prevention of nausea and vomiting associated with highly emetogenic chemotherapy**<br>24 mg PO given 30 min prior to start of single-day chemotherapy | PO: 24 mg/day<br>IV: 16 mg/dose (up to 3 doses/day) |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| | **Prevention of nausea and vomiting associated with emetogenic chemotherapy**<br>0.15 mg/kg/dose IV given 30 min prior to chemotherapy, then repeat dose 4 and 8 hrs after initial dose<br><br>**Treatment of nausea and vomiting associated with chemotherapy***<br>16 to 24 mg PO daily or 8 to 16 mg IV<br><br>**Prevention of nausea and vomiting associated with radiation therapy**<br>Total body irradiation: 8 mg PO given 1 to 2 hrs prior to each daily fraction of radiotherapy<br>Single high-dose radiotherapy: 8 mg PO given 1 to 2 hrs prior to irradiation, then 8 mg PO Q8H for 1 to 2 days after completion of radiotherapy<br>Daily fractionated radiotherapy: 8 mg PO given 1 to 2 hrs prior to irradiation, then 8 mg PO Q8H for each day of radiotherapy<br><br>**Prevention of PONV**<br>16 mg PO given 1 hr prior to anesthesia or 4 mg IM/IV as a single dose given 30 min before end of anesthesia<br><br>**Treatment of PONV***<br>4 mg IV as a single dose | |

*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): known hypersensitivity to the drug or its components
- 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.

## V. Dosage and Administration

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| **Drug Name** | **Indication** | **Dosing Regimen** | **Maximum Dose** |
| Granisetron (Kytril®) | Prevention of nausea and vomiting associated with cancer chemotherapy | 2 mg PO QD or 1 mg PO BID given 1 hr prior to chemotherapy or 10 mcg/kg IV given within 30 min of chemotherapy | PO: 2 mg/day<br>IV: 10 mcg/kg/day |
| Granisetron (Kytril®) tablet | Prevention of nausea and vomiting associated with radiotherapy | 2 mg PO QD given within 1 hr of radiation | 2 mg/day |
| Granisetron (Kytril®) injection | Prevention and treatment of postoperative nausea and vomiting | 1 mg IV given before anesthesia or immediately after anesthesia | 1 mg/dose |
| Granisetron (Sancuso®) | Prevention of nausea and vomiting associated with cancer chemotherapy | Apply 1 patch to upper outer arm 24 to 48 hrs prior to chemotherapy; | 1 patch/7 days |

| | | | |
|---|---|---|---|
| | | Remove patch at least 24 hrs after completion of chemotherapy | |
| Granisetron (Sustol®) | Prevention of nausea and vomiting associated with cancer chemotherapy | 10 mg SC 30 minutes prior to the initiation of MED or AC combination chemotherapy on Day 1. | 10 mg/7 days |

## VI. Product Availability

| Drug Name | Availability |
|---|---|
| Granisetron (Kytril®) | Tablets: 1 mg<br>Injection: 0.1 mg/mL, 1 mg/mL |
| Granisetron (Sancuso®) | Transdermal system: 3.1 mg/24 hours |
| Granisetron (Sustol®) | Extended-release pre-filled syringe: 10 mg/0.4 mL |

## VII. References

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| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| 4Q 2018 annual review: removed Granisol due to product discontinuation; generalized trial and failure for all indications to any 5-$HT_3$ antagonist (ondansetron is preferred), modified approval duration for PONV to one time approval and chemo- or radiation therapy-induced N/V to duration of therapy up to 72 and 48 hrs respectively; policy split from PA.CP.PMN.11 Oral antiemetics into individual policies, into individual policies, removed age restriction for Kytril due to compendium and guideline-supported off-label use in pediatrics, removed requirement that ondansetron must have been tried in the last 60 days, added granisetron injection product to policy; references reviewed and updated. | 08/18 | |
| 1Q 2019 annual review: references reviewed and updated. | 01/19 | |