

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

Reference Number: CP.PMN.74

Effective Date: 11.01.16

Last Review Date: 11.18

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**

Granisetron (Kytril<sup>®</sup>, Sancuso<sup>®</sup>, Sustol<sup>®</sup>) is a serotonin (5-HT<sub>3</sub>) receptor antagonist.

### **FDA Approved Indication(s)**

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 days 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 cyclophosphamide (AC) combination chemotherapy regimens.

### **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<sup>®</sup> that Kytril, Sancuso, and Sustol are **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 prevention or treatment of chemotherapy-induced nausea/vomiting;
2. For Sancuso or Sustol: Age ≥ 18 years;
3. Member is scheduled to receive cancer chemotherapy (*see Appendix D*);

4. Failure of a formulary 5-HT<sub>3</sub> receptor antagonist (*ondansetron is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a, b, c, or d):
  - a. Tablet: Dose does not exceed 2 mg per day;
  - b. IV injection: Dose does not exceed 10 mcg/kg per day;
  - c. SC injection: 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. Age ≥ 18 years;
4. Member is scheduled to receive radiation therapy;
5. Failure of a formulary 5-HT<sub>3</sub> receptor antagonist (*ondansetron is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. 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 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<sub>3</sub> 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<sub>3</sub> 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: one time approval (3 days)**

**D. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

## II. Continued Therapy

### A. Postoperative Nausea and Vomiting (must meet all):

Reauthorization is not permitted. Members will need to be re-evaluated using initial approval criteria.

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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, or d):
  - a. Tablet: New dose does not exceed 2 mg per day;
  - b. Injection: New dose does not exceed 10 mcg/kg per day;
  - c. SC injection: 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 Centene benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 12 months (whichever is less); or**

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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<sub>3</sub>: 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.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
<b>5-HT<sub>3</sub> Serotonin Antagonists</b>		
Akynzeo <sup>®</sup> (fosnetupitant/ palonosetron)	<b>Prevention of nausea and vomiting associated with highly emetogenic chemotherapy</b> 1 vial IV given 30 min prior to chemotherapy on day 1	1 vial/chemotherapy cycle
Akynzeo <sup>®</sup> (netupitant/ palonosetron)	<b>Prevention of nausea and vomiting associated with highly emetogenic chemotherapy</b> 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 <sup>®</sup> (dolasetron)	<b>Prevention of nausea and vomiting associated with chemotherapy</b> 100 mg PO within 1 hr prior to chemotherapy	100 mg/day
Aloxi <sup>®</sup> (palonosetron)	<b>Prevention of nausea and vomiting associated with chemotherapy</b> 0.25 mg IV given 30 min prior to chemotherapy  <b>Prevention of PONV</b> 0.075 mg IV given immediately prior to anesthesia	Chemo-induced N/V prophylaxis: 0.25 mg/day PONV prophylaxis: 0.075 mg/day
ondansetron (Zofran <sup>®</sup> , Zofran <sup>®</sup> ODT, Zuplenz <sup>®</sup> )	<b>Prevention of nausea and vomiting associated with moderately emetogenic chemotherapy</b> <u>Age 12 years or older:</u> 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 <u>Age 4 to 11 years:</u> 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	PO: 24 mg/day IV: 16 mg/dose (up to 3 doses/day)

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

Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

\*Off-label

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Sustol is contraindicated in patients with hypersensitivity to granisetron, any of the components of Sustol, or to any of the other 5-HT<sub>3</sub> receptor antagonists.

- Kytil Injection is contraindicated in patients with known hypersensitivity to the drug or to any of its components.
- Sancuso is contraindicated in patients with known hypersensitivity to granisetron or to any of the components of the patch.
- 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<sub>3</sub> receptor antagonist (recommended by NCCN only). NK<sub>1</sub> receptor antagonists are not included in low risk antiemetic recommendations.
- Moderate emetic risk chemotherapy: 5-HT<sub>3</sub> receptor antagonists and dexamethasone may be used in combination and with or without NK<sub>1</sub> 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<sup>2</sup>, cytarabine < 1,000 mg/m<sup>2</sup>, daunorubicin, doxorubicin, epirubicin, idarubicin, ifosfamide, irinotecan, oxaliplatin
- High emetic risk chemotherapy: NK<sub>1</sub> receptor antagonists are recommended for use in combination with 5-HT<sub>3</sub> receptor antagonists and dexamethasone. Olanzapine may also be used in combination with 5-HT<sub>3</sub> receptor antagonists, dexamethasone, and/or NK<sub>1</sub> receptor antagonists.
  - Examples of high emetic risk chemotherapy: carmustine, cisplatin, cyclophosphamide ≥ 1,500 mg/m<sup>2</sup>, 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<sub>3</sub> receptor antagonists (dolasetron, ondansetron, granisetron), steroids (dexamethasone), or (haloperidol, metoclopramide, scopolamine). An NK<sub>1</sub> receptor antagonist may be added to the prophylaxis regimen of the next chemotherapy cycle if not previously included.

**V. Dosage and Administration**

<b>Drug Name</b>	<b>Indication</b>	<b>Dosing Regimen</b>	<b>Maximum Dose</b>
Granisetron (Kytril <sup>®</sup> )	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 IV: 10 mcg/kg/day
Granisetron (Kytril <sup>®</sup> ) tablet	Prevention of nausea and vomiting	2 mg PO QD given within 1 hr of radiation	2 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
	associated with radiotherapy		
Granisetron (Kytril <sup>®</sup> ) injection	Prevention and treatment of postoperative nausea and vomiting	1 mg IV given before anesthesia or immediately after anesthesia	1 mg/dose
Granisetron (Sancuso <sup>®</sup> )	Prevention of nausea and vomiting associated with cancer chemotherapy	Apply 1 patch to upper outer arm 24 to 48 hrs prior to chemotherapy; Remove patch at least 24 hrs after completion of chemotherapy	1 patch/7 days
Granisetron (Sustol <sup>®</sup> )	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 <sup>®</sup> )	Tablets: 1 mg Injection: 0.1 mg/mL, 1 mg/mL
Granisetron (Sancuso <sup>®</sup> )	Transdermal system: 3.1 mg/24 hours
Granisetron (Sustol <sup>®</sup> )	Extended-release pre-filled syringe: 10 mg/0.4 mL

#### VII. References

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8. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: <http://www.clinicalpharmacology-ip.com/>.
9. Micromedex<sup>®</sup> Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 15, 2018.

**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
J1626	Injection, granisetron hydrochloride, 100 mcg
Q0166	Granisetron hydrochloride, 1 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 24 hour dosage regimen
S0091	Granisetron hydrochloride, 1 mg (for circumstances falling under the Medicare statute, use Q0166)
J1627	Injection, granisetron extended release, 0.1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created. Sancuso was removed from CP.PMN.11 Oral Antiemetics policy because sancuso is not an oral product. All references to radiation therapy were removed as Sancuso is not approved for use in radiation.	08.16	11.16
Added age per PI. Verified and updated references.	07.01.17	11.17
3Q 2018 annual review: policies combined for commercial, and Medicaid lines of business; removed Granisol due to product discontinuation; For commercial: policy split from CP.CPA.223 Antiemetics – 5-HT <sub>3</sub> Receptor Antagonist into individual policies, added age requirement for Sancuso, generalized trial and failure for all indications to any 5-HT <sub>3</sub> 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; For Medicaid: policy split from 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.	05.15.18	08.18



Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added Sustol to the policy; references reviewed and updated.	09.04.18	11.18

**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.

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**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.

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