RXADVANCE
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Southborough, MA 01772

Clinical Policy Title:	granisetron
Policy Number:	RxA.184
Drug(s) Applied:	Sancuso®, Sustol®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of Business

Background

Granisetron is a serotonin (5-HT_3) receptor antagonist that is indicated for prevention of chemotherapy-associated nausea and vomiting. In addition, granisetron tablet is indicated for prophylaxis of radiation therapy-associated emesis. Granisetron IV is used off-label for prevention of postoperative nausea and vomiting.

Sancuso® (granisetron) 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® (granisetron) 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum 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; Remove patch at least 24 hrs after completion of chemotherapy	1 patch/7 days
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
Granisetron hydrochloride Tablet	Prevention of nausea and vomiting associated with cancer chemotherapy	2 mg ORALLY 1 hour before chemotherapy or 1 mg ORALLY 1 hour before and 1 mg 12 hours after chemotherapy.	2mg/day/ chemotherapy session
Granisetron hydrochloride Intravenous	Prevention of nausea and vomiting associated with cancer chemotherapy	10 mcg/kg IV 30 minutes before chemotherapy.	10 mcg/kg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
Granisetron hydrochloride Intravenous	PONV	0.35 to 3 mg or 5 to 20 mcg/kg administered at the end of surgery	3mg/ day/ chemotherapy session

Dosage Forms

- Granisetron (Sancuso®) transdermal system: 3.1 mg/24 hours
- Granisetron (Sustol®) extended-release pre-filled syringe: 10 mg/0.4 mL
- Granisetron hydrochloride oral tablet: 10 mg
- Granisetron hydrochloride intravenous: 1 mg/mL, 4mg/4mL

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 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*); 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. 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

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

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

a. Request is for granisetron tablet;
b. Prescribed for the prevention of radiation-induced nausea/vomiting;
c. Age ≥ 18 years;
d. Member is scheduled to receive radiation therapy;
e. 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;
f. Dose does not exceed 2 mg per day.

Approval Duration

Commercial: projected course of radiation therapy up to 48 hours after completion of radiation therapy

Medicaid: projected course of radiation therapy up to 48 hours after completion of radiation therapy

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

a. Request is for granisetron IV injection;
b. Age ≥ 18 years;
c. Prescribed for the prevention or treatment of postoperative nausea/vomiting;
d. Member is scheduled to undergo surgery;
e. Member meets one of the following (i or ii):
i. 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;
ii. For treatment: Member did not receive a preoperative 5-HT_3 receptor antagonist (e.g., ondansetron);
f. Request meets one of the following (i or ii):
i. Dose does not exceed 3 mg once;
ii. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval Duration
Commercial: one time approval (7 days)
Medicaid: one time approval (7 days)

II. Continued Therapy Approval

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 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 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. IV Injection: New dose does not exceed 10 mcg/kg per day;
   c. SC injection: Dose does not exceed 10 mg per 7 days;
   d. Transdermal: 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
Commercial: projected course of chemotherapy up to 72 hours after completion of chemotherapy or projected course of radiation therapy up to 48 hours after completion of radiation therapy
Medicaid: projected course of chemotherapy up to 72 hours after completion of chemotherapy or projected course of radiation therapy up to 48 hours after completion of radiation therapy

III. Appendices

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 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)	1 capsule or vial/chemotherapy cycle
Anzemet® (dolasetron)	**Prevention of nausea and vomiting associated with chemotherapy** 100 mg PO within 1 hr prior to chemotherapy	100 mg/day
Aloxi® (palonosetron)	**Prevention of nausea and vomiting associated with chemotherapy** 0.25 mg IV given 30 min prior to chemotherapy **Prevention of PONV** 0.075 mg IV given immediately prior to anesthesia	Chemo-induced Nausea/Vomiting prophylaxis: 0.25 mg/day PONV prophylaxis: 0.075 mg/day
ondansetron (Zofran®, 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	PO: 24 mg/day IV: 16 mg/dose (up to 3 doses/day)

	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 **Prevention of nausea and vomiting associated with radiation therapy** Total body irradiation: 8 mg PO given 1 to 2 hrs prior to each daily fraction of radiotherapy 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 Daily fractionated radiotherapy: 8 mg PO given 1 to 2 hrs prior to irradiation, then 8 mg PO Q8H for each day of radiotherapy **Prevention of PONV** 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 **Treatment of PONV*** 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):
  - Sustol is contraindicated in patients with hypersensitivity to granisetron, any of the components of Sustol, or to any of the other 5-HT3 receptor antagonists.
  - 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: 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 $5HT_3$ 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/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-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

1. Sancuso Prescribing Information. Bedminster, NJ: Kyowa Kirin, Inc.; April 2020. Available at http://sancuso.com/hcp/share/pdf/SANCUSO-Full_PI.pdf. Accessed June 26, 2020.
2. Sustol Prescribing Information. San Diego, CA: Heron Therapeutics; May 2017. Available at: https://www.sustol.com/public/pdfs/PI-May2017.pdf 0. Accessed June 26, 2020.
3. Gan TJ, Diemunsch, P, Habib AS, et al, Society for Ambulatory Anesthesia Guidelines for the Management of Postoperative Nausea and Vomiting. Anesth Analg 2014; 118:85-113.

4. Hesketh, PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 2017: JCO2017744789.
5. National Comprehensive Cancer Network. Antiemesis Version 2.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed June 26, 2018.
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/.
7. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed June 26, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Drug(s) Applied was updated: Kytril was removed due to drug discontinuation. 3. Line of Business Policy Applies to was updated to all lines of business. 4. Background was updated. 5. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance...". 6. Dosing information updated to include oral and IV dose regimen for Nausea and Vomiting Associated with Cancer Chemotherapy and IV dose regimen for Postoperative Nausea/Vomiting, respectively. 7. Initial and Continued Approval Duration was updated to included Medicaid approval duration. 8. Initial approval duration for Postoperative Nausea/Vomiting was updated from one time (3 days) to one time (7 days). 9. Criteria I.C.f.i was updated from 1 mg to 3 mg. 10. APPENDIX B was updated: brand Zofran®ODT was removed due to drug discontinuation. 11. References were updated.	06/26/2020	09/14/2020