09-J0000-97

Original Effective Date: 04/15/09

Reviewed: 03/12/25

Revised: 04/15/25

Subject: Granisetron (Sustol®) Injection

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DESCRIPTION:

Chemotherapy induced (or radiation therapy induced) vomiting and nausea can significantly affect a patient's quality of life, leading to poor compliance with further chemotherapy or radiation therapy treatment. The severity and incidence of chemotherapy or radiation therapy induced nausea and vomiting are affected by factors such as the selected agent and dose of chemotherapy, route of administration, location of radiation therapy, prior chemotherapy use, and patient age and sex.

In general, to provide maximal protection against chemotherapy induced nausea and vomiting, antiemetic therapy should be initiated before chemotherapy. The antiemetic therapy should also be continued for the same length of time as the duration of the emetic activity of the chemotherapeutic agent being used. However, daily use of antiemetics is not recommended for some therapeutic agents that are taken long term (e.g., imatinib, erlotinib). Antiemetic agents can be administered by the oral, rectal, IV, intramuscular, subcutaneous or transdermal route.

Granisetron (Kytril) injection was approved by the U.S. Food and Drug Administration (FDA) in December 1993 for prevention of nausea and vomiting associated with cancer chemotherapy. Granisetron selectively blocks serotonin 5-HT3 receptors to prevent emesis. A subcutaneous formulation of granisetron (Sustol) was FDA approved in August 2016 for use 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 (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens. In a randomized, multicenter, double-blind study of patients receiving moderately emetogenic chemotherapy, a 10 mg granisetron delayed-release subcutaneous injection was noninferior to palonosetron 0.25 mg IV regarding a complete response (no emetic episodes and no rescue therapy needed). Granisetron delayed-release subcutaneous injection also

demonstrated noninferiority to palonosetron regarding a complete response in patients receiving chemotherapy regimens with an anthracycline plus cyclophosphamide.

National Comprehensive Cancer Network (NCCN) Guidelines for antiemesis recommend granisetron subcutaneous injection for acute and delayed emesis prevention in combination with a NK1 antagonist (e.g., aprepitant, fosaprepitant, rolapitant) and dexamethasone before intravenous antineoplastic therapy with high or moderate emetic risk. It is also recommended in combination with dexamethasone without an NK1 antagonist for chemotherapy with moderate emetic risk. It is also recommended in combination with a NK1 antagonist (e.g., aprepitant, fosaprepitant, rolapitant), olanzapine, and dexamethasone for high risk antineoplastic therapy or if emesis occurred during a previous cycle of antineoplastic therapy with a 3-drug regimen.

POSITION STATEMENT:

Granisetron (Sustol®) subcutaneous **meets the definition of medical necessity** for members meeting **ALL** of the following criteria:

1. Use is for **ONE** of the following:
    a. Prevention of acute or delayed chemotherapy induced nausea and vomiting associated with initial or repeat courses of moderately emetogenic chemotherapy (see Table 1)
    b. Prevention of acute or delayed chemotherapy induced nausea and vomiting associated with initial or repeat courses of highly emetogenic chemotherapy (see Table 1) and use is in combination with an NK1 antagonist (e.g., fosaprepitant, aprepitant, rolapitant) or the member has a contraindication or intolerance to an NK1 antagonist
    c. Prevention of acute or delayed chemotherapy induced nausea and vomiting associated with initial or repeat courses of low emetogenic chemotherapy (Table 1) and the member had an inadequate response or contraindication to use of an alternative formulation of a serotonin antagonist (e.g., oral ondansetron, granisetron)† to prevent chemotherapy-induced nausea and vomiting with the current regimen.
2. The member had an inadequate response or contraindication to palonosetron†
3. Use is in combination with dexamethasone or the member has a contraindication or intolerance to dexamethasone*
4. Member is not receiving an additional serotonin antagonist (e.g., palonosetron, granisetron transdermal)
5. Dose does not exceed 10 mg every 7 days.

Approval Duration: 6 months

*Note: Given with or without olanzapine, lorazepam, histamine-2 receptor blocker or proton pump inhibitor

†Step therapy requirement does not apply if the member was previously approved by Florida Blue or a prior health plan

DOSAGE/ADMINISTRATION:

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FDA-approved

Granisetron SQ: 10 mg administered subcutaneously in combination with dexamethasone at least 30 minutes before the initiation of MEC or AC combination chemotherapy. Administer on Day 1 of chemotherapy and not more frequently than once every 7 days because of the extended-release properties of the formulation. See the prescribing information for the recommended administration technique and dexamethasone dosage.

Dose Adjustments

Granisetron SQ:

- Moderate renal impairment (CrCl 30 to 59 mL/min): administer on Day 1 of chemotherapy and not more frequently than once every 14 days
- Severe renal impairment (CrCl less than 30 mL/min): avoid use.

Drug Availability

Granisetron SQ:

- Extended-Release Injection: 10 mg/0.4 mL in a single-dose pre-filled syringe.

PRECAUTIONS:

Contraindications:

- Granisetron SQ: Hypersensitivity to granisetron, any of the components of the formulation, or to any of the other 5-HT receptor antagonists.

Precautions/Warnings:

Granisetron SQ:

- Injection site reactions, including infection, bleeding, pain, nodules, swelling and induration may occur. Note that some may occur 2 weeks or more after administration.
- Increased risk of bruising or severe hematoma in patients receiving anticoagulants or antiplatelet agents.
- Gastrointestinal disorders: Monitor for constipation or decreased bowel activity, and signs and symptoms of ileus.
- Hypersensitivity reactions: Serious reactions have been reported and may occur up to 7 days or longer following administration.

- Serotonin syndrome may occur particularly with concomitant use of serotonergic drugs.

BILLING/CODING INFORMATION:

HCPCS Coding:

J1627	Injection, granisetron, extended-release, 0.1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity for granisetron SQ (Sustol)(C9399, J3490):

R11.0	Nausea
R11.10 – R11.12	Vomiting, unspecified
R11.2	Nausea with vomiting, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs, sequela
T45.95XA	Adverse effect of unspecified primarily systemic and hematological agent, initial encounter
T50.905A	Adverse effect of unspecified drugs, medicaments and biological substances
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT.**

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

No guideline specific definitions apply.

RELATED GUIDELINES:

Aprepitant injectable therapy (Cinvanti), 09-J2000-60
Fosnetupitant-palonosetron (Akynzeo), 09-J3000-01

OTHER:

Table 1

Emetogenic Potential of Antineoplastic Agents		
	High emetic risk (>90% frequency of emesis)	**Moderate emetic risk (30-90% frequency of emesis)**
IV	AC combination (doxorubicin or epirubicin with cyclophosphamide) Carboplatin AUC ≥ 4 Carmustine (>250 mg/m2) Cisplatin Cyclophosphamide (> 1500 mg/m2) Dacarbazine Doxorubicin (≥60 mg/m2) Epirubicin (>90 mg/ m2) Fam-trastuzumab deruxtecan-nxki Ifosfamide (≥2 g/ m2) Mechlorethamine Melphalan (≥ 140 mg/m2) Sacituzumab govitecan-hziy Streptozocin	Aldesleukin (>12-15 million IU/m2) Amifostine (>300 mg/m2) Bendamustine Busulfan Carboplatin AUC < 4 Carmustine (≤250 mg/m2) Clofarabine Cyclophosphamide (≤1500 mg/m2) Cytarabine (>200 mg/m2) Dactinomycin Daunorubicin Dinutuximab Doxorubicin (<60 mg/m2) Dual-drug liposomal encapsulation of cytarabine and daunorubicin Epirubicin (≤90 mg/m2) Idarubicin Ifosfamide (< 2g/m2) Irinotecan Irinotecan (liposomal) Lurbinectedin Melphalan (< 140 mg/m2) Methotrexate (≥250 mg/m2) Mirvetuximab soravtansine-gynx Naxitamab-gqgk Oxaliplatin Romidepsin Temozolomide Trabectedin
IV	**Low emetic risk (10 – 30% frequency of emesis)**	

	Ado-trastuzumab emtansine Aldesleukin ≤ 12 million international units/m^2 Amifostine ≤ 300 mg/m^2 Amivantamab-vmjw Arsenic trioxide Axicabtagene ciloleucel Azacitidine Belinostat Brexucabtagene autoleucel Brentuximab vedotin Cabazitaxel Carfilzomib Ciltacabtagene autoleucel Copanlisib Cytarabine (low dose) 100 – 200 mg/m^2 Docetaxel Doxorubicin (liposomal) Enfortumab vedotin-ejfv Eribulin Etoposide 5-FU Floxuridine Gemcitabine Gemtuzumab ozogamicin Idecabtagene vicleucel Inotuzumab ozogamicin Isatuximab-irfc Ixabepilone Lisocabtagene maraleucel Loncastuximab tesirine-lpyl Methotrexate > 50 mg/m2 - <250 mg/m^2 Mitomycin Mitomycin pyelocalyceal solution Mitoxantrone Mogamulizumab-kpkc Mosunetuzumab-axgb Necitumumab Omacetaxine Paclitaxel Paclitaxel-albumin Pemetrexed Pentostatin Polatuzumab vedotin-piig Pralatrexate

	Tafasitamab-cxix Tagraxofusp-erzs Talimogene laherparepvec Tebentafusp-tebn Thiotepa Tisagenlecleucel Tisotumab vedotin-tftv Topotecan Ziv-aflibercept

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 03/12/25.

GUIDELINE UPDATE INFORMATION:

04/15/09	New Medical Coverage Guideline.
10/15/09	Revision; consisting of clarifying dosage.
01/01/10	Revision; consisting of adding fixed dosing as an alternative in position statement.
09/15/10	Review and revision; consisting of updating references.
01/15/11	Revision to guideline; consisting of adding ICD-10 codes.
09/15/11	Review and revision to guideline; consisting of updating coding and references.
09/15/12	Review and revision to guideline; consisting of removing postanesthetic shivering indication, reformatting position statement, updating coding and references.
08/15/13	Review and revision to guideline; consisting of description, position statement, dosage/administration, precautions, program exceptions, and references.

11/01/15	Revision: ICD-9 Codes deleted.
11/15/16	Review and revision to guideline; consisting of updating description, position statement, dosage/administration, precautions, coding and references.
12/15/16	Revision to guideline; consisting of updating position statement, description, dosage/administration, precautions, coding and references.
04/01/17	Revision to guideline consisting of adding HCPCS code C9486.
09/15/17	Review and revision to guideline; consisting of updating position statement, description, and references.
10/15/17	Revision to guideline; consisting of updating position statement, description, and references.
01/01/18	Annual HCPCS coding update: added HCPCS code J1627 and deleted code C9486.
05/15/19	Review and revision to guideline; consisting of updating position statement, Table 1, and references.
01/01/20	Revision to guideline; consisting of updating the position statement.
05/15/20	Revision to guideline; consisting of updating Table 1 and references.
05/15/21	Review and revision to guideline; consisting of updating Table 1 and references.
05/15/22	Review and revision to guideline; consisting of updating Table 1, description, and references.
04/15/23	Review and revision to guideline; consisting of updating Table 1 (Emetic potential of neoplastic agents) and references.
04/15/24	Review and revision to guideline; consisting of updating Table 1 (Emetic potential of neoplastic agents) and references.
04/15/25	Review and revision to guideline; consisting of updating the references.