DRUG QUANTITY MANAGEMENT POLICY – PER RX

POLICY: Antiemetics – Serotonin Receptor Antagonists (Oral and Transdermal) Drug Quantity Management – Per Rx

- granisetron tablets (generic only)
- Sancuso® (granisetron transdermal system – Kyowa Kirin)
- Zofran® (ondansetron tablets – Novartis, generic)
- ondansetron orally disintegrating tablets (generic only)
- ondansetron oral solution (generic only)
- Zuplenz® (ondansetron oral soluble film – Aquestive)

REVIEW DATE: 12/05/2022

OVERVIEW

Indications and Dosing/Availability

All of the oral serotonin (5-HT_3) receptor antagonists have similar indications regarding the prevention of nausea/vomiting associated with emetogenic cancer chemotherapy.[1-5] Details, additional indications, and recommended dosing are in Table 1.

Table 1. Indications and Dosages for Oral and Transdermal 5-HT_3 Receptor Antagonists.[1-5]

Drug/ Availability	FDA-Approved Indications	Recommended Dosage
Granisetron 1 mg tablets	Prevention of nausea/vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.	***Adults:*** 2 mg QD or 1 mg BID. In the 2-mg QD regimen, two 1-mg tablets are given up to 1 hour before chemotherapy. In the 1-mg BID regimen, the first 1-mg tablet is given up to 1 hour before chemotherapy, with the second tablet 12 hours after the first. Either regimen is given only on the day(s) of chemotherapy. Continued treatment, while not on chemotherapy, has not been found to be useful. ***Pediatric:*** Safety and efficacy of granisetron in pediatric patients have not been established.
	Prevention of nausea/vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.	***Adults:*** 2 mg QD. Two 1-mg tablets are taken within 1 hour of radiation. ***Pediatric:*** Safety and efficacy of granisetron in pediatric patients have not been established.
Sancuso® (granisetron 3.1 mg/24 hours transdermal system)	Prevention of nausea/vomiting associated with MEC or HEC regimens of up to 5 consecutive days' duration.	***Adults:*** Apply a single patch to the upper arm a minimum of 24 hours before chemotherapy and a maximum of 48 hours prior to chemotherapy as appropriate. The patch can be worn for up to 7 days depending upon the duration of the chemotherapy regimen. Remove a minimum of 24 hours after completion of chemotherapy. ***Pediatric:*** Safety and efficacy of Sancuso in pediatric patients have not been established.

Table 1 (continued). Indications and Dosages for Oral and Transdermal 5-HT$_3$ Receptor Antagonists.[1-5]

Drug/ Availability	FDA-Approved Indications	Recommended Dosage
Zofran® (ondansetron 4 mg and 8 mg tablets and 4 mg/5 mL oral solution, generics) ondansetron 4 mg and 8 mg orally disintegrating tablets (generic only) Zuplenz® (ondansetron 4 mg and 8 mg oral soluble film) Ondansetron 24 mg tablets	Prevention of nausea/vomiting associated with HEC, including cisplatin ≥ 50 mg/m2.	***Adults:*** 24 mg given as three 8-mg tablets (or films) given 30 minutes before the start of single-day highly emetogenic chemotherapy, including cisplatin ≥ 50 mg/m^2. Multi-day, single-dose administration of 24-mg dosage has not been studied.
	Prevention of nausea/vomiting associated with initial and repeat courses of MEC.	***Adults:*** 8 mg BID. The first dose should be taken 30 minutes before the start of emetogenic chemotherapy, with a subsequent dose 8 hours after the first dose. The 8-mg dose should be taken BID (Q12H) for 1 to 2 days after completing chemotherapy. ***Pediatric (≥12 years):*** 8 mg BID. 8 mg administered 30 minutes before the start of chemotherapy, with a subsequent 8-mg dose 8 hours after the first dose, then administer 8 mg BID for 1 to 2 days after completion of chemotherapy. ***Pediatric (4 to 11 years):*** 4 mg TID. The first dose should be taken 30 minutes before the start of chemotherapy, with subsequent doses 4 and 8 hours after the first. The 4-mg dose should be given TID (Q8H) for 1 to 2 days after completion of chemotherapy.
	Prevention of nausea/vomiting associated with radiotherapy in patients receiving total body irradiation, a single high-dose fraction to the abdomen, or daily fractions to the abdomen.	***Total body irradiation:*** 8 mg 1 to 2 hours before each fraction of radiotherapy each day. ***Single high-dose fractionated radiotherapy to the abdomen:*** 8 mg 1 to 2 hours before radiotherapy, with subsequent doses Q8H after the first dose for 1 to 2 days after completion of radiotherapy. ***Daily fractionated radiotherapy to the abdomen:*** 8 mg 1 to 2 hours before radiotherapy with subsequent doses Q8H after the first, each day of radiotherapy.
	Prevention of PONV. As with other antiemetics, routine prophylaxis is not recommended for patients in whom there is little expectation that nausea/vomiting will occur. For patients in whom PONV must be avoided, ondansetron is recommended even where the incidence of PONV is low.	16 mg given as two 8-mg tablets (or films) one hour before induction of anesthesia.

HEC – Highly emetogenic chemotherapy; CINV – Chemotherapy-induced nausea and vomiting; AC – Anthracycline and cyclophosphamide; MEC – Moderately emetogenic chemotherapy; PONV – Post-operative nausea and vomiting; BID – Twice daily; Q12H – Every 12 hours; TID – Three times daily; Q8H – Every 8 hours; QD – Once daily.

POLICY STATEMENT

This Drug Quantity Management program has been developed to promote the safe, effective, and economic use of the serotonin receptor antagonists (oral and transdermal). If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration, unless otherwise noted below.

Automation: None.

Drug Quantity Limits

Product	Strength	Retail Maximum Quantity per Rx	Home Delivery Maximum Quantity per Rx
granisetron (generic only)	1 mg tablets	6 tablets	18 tablets
Sancuso® (granisetron transdermal system)	34.3 mg (3.1 mg/24 hours) transdermal system (patch)	1 patch	3 patches
Zofran® (ondansetron tablets, generic)	4 mg tablets	9 tablets	27 tablets
	8 mg tablets	9 tablets	27 tablets
ondansetron 24 mg tablets (generic only)	24 mg tablets	1 tablet	3 tablets
ondansetron orally disintegrating tablets (generic only)	4 mg tablets	9 tablets	27 tablets
	8 mg tablets	9 tablets	27 tablets
ondansetron oral solution (generic only)	4 mg/5 mL solution (50 mL bottles)	100 mL (2 bottles)	300 mL (4 bottles)
Zuplenz® (ondansetron oral soluble film)	4 mg soluble film	10 films	30 films
	8 mg soluble film	10 films	30 films

CRITERIA

Granisetron 1 mg tablets (generic only)

1. If the patient is receiving granisetron for the *prevention* of nausea and vomiting associated with multiple courses or multiple days of cancer chemotherapy within 1 month, approve the requested quantity, not to exceed a total of 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery.

2. If the patient is receiving granisetron for the treatment of one of the following conditions, approve the requested quantity, not to exceed 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery (i.e., allow for two tablets per day), for 6 months:
- prevention or treatment of radiation-induced emesis,
- delayed nausea and vomiting (greater than 24 hours following chemotherapy or radiation therapy),
- as needed for nausea and vomiting after chemotherapy,
- anticipatory nausea and vomiting,
- vertigo or motion-induced nausea and vomiting,
- opioid-induced nausea and vomiting,
- treatment of postoperative nausea and vomiting,
- pregnancy-induced nausea and vomiting,
- drug-induced (non-chemotherapy) nausea and vomiting, or
- nausea and vomiting due to other etiologies including idiopathic.

Sancuso 34.3 mg (3.1 mg/24 hours) Transdermal System

1. If the patient is receiving Sancuso for the *prevention* of nausea and vomiting associated with multiple courses or multiple days of cancer chemotherapy within 1 month, approve the quantity requested, not to exceed a total of 4 patches per dispensing at retail or 16 patches per dispensing at home delivery.

Ondansetron 4 mg tablets (Zofran, generic), Ondansetron 4 mg orally-disintegrating tablets, Zuplenz 4 mg soluble film

1. If the patient is receiving ondansetron (Zofran, generic) or Zuplenz for the *prevention* of nausea and vomiting associated with multiple courses or multiple days of chemotherapy within 1 month, approve the requested quantity, not to exceed 90 tablets/orally-disintegrating tablets/films per dispensing at retail or 270 tablets/orally-disintegrating tablets/films per dispensing at home delivery.

2. If the patient is receiving ondansetron (Zofran, generic) or Zuplenz for the *prevention* of radiation-induced nausea and vomiting associated with multiple courses or multiple days of radiation within 1 month, approve the requested quantity, not to exceed 90 tablets/orally-disintegrating tablets/films per dispensing at retail or 270 tablets/orally-disintegrating tablets/films per dispensing at home delivery.

3. If the patient is receiving ondansetron (Zofran, generic) or Zuplenz for pregnancy-induced nausea and vomiting, approve the requested quantity, not to exceed 90 tablets/orally-disintegrating tablets/films per dispensing at retail or 270 tablets/orally-disintegrating tablets/films per dispensing at home delivery (i.e., three tablets/orally-disintegrating tablets/films per day) for 6 months.

4. If the patient is receiving ondansetron (Zofran, generic) or Zuplenz for the treatment of one of the following conditions, approve the requested quantity, not to exceed 60 tablets/orally-disintegrating tablets/films per dispensing at retail or 180 tablets/orally-disintegrating tablets/films per dispensing at home delivery (i.e., allow for two tablets/orally-disintegrating tablets/films per day), for 6 months:
- treatment of radiation-induced emesis,
- delayed nausea and vomiting (greater than 24 hours following chemotherapy or radiation therapy),
- as needed for nausea and vomiting after chemotherapy,
- anticipatory nausea and vomiting,
- vertigo or motion-induced nausea and vomiting,
- opioid-induced nausea and vomiting,
- treatment of postoperative nausea and vomiting,
- drug-induced (non-chemotherapy) nausea and vomiting, or
- nausea and vomiting due to other etiologies including idiopathic.

Ondansetron 8 mg tablets (Zofran, generic), Ondansetron 8 mg orally-disintegrating tablets, Zuplenz 8 mg soluble film

1. If the patient is ≥ 12 years of age and is receiving ondansetron (Zofran, generic) or Zuplenz for the *prevention* of nausea and vomiting associated with multiple courses or multiple days of chemotherapy within 1 month, approve the requested quantity, not. to exceed 90 tablets/orally-disintegrating tablets/films per dispensing at retail or 270 tablets/orally-disintegrating tablets/films per dispensing at home delivery.

2. If the patient is ≥ 12 years of age and is receiving ondansetron (Zofran, generic) or Zuplenz for the *prevention* of radiation-induced nausea and vomiting associated with multiple courses or multiple days of radiation within 1 month, approve the requested quantity not to exceed 90 tablets/orally-disintegrating tablets/films per dispensing at retail or 270 tablets/orally-disintegrating tablets/films per dispensing at home delivery.

3. If the patient is receiving ondansetron (Zofran, generic) or Zuplenz for pregnancy-induced nausea and vomiting, approve the requested quantity, not to exceed 90 tablets/orally-disintegrating tablets/films per dispensing at retail or 270 tablets/orally-disintegrating tablets/films per dispensing at home delivery (i.e., three tablets/orally-disintegrating tablets/films per day) for 6 months.

5. If the patient is ≥ 12 years of age AND is receiving ondansetron (Zofran, generic) or Zuplenz for the treatment of one of the following conditions, approve the requested quantity, not to exceed 60 tablets/orally-disintegrating tablets/films per dispensing at retail or 180 tablets/orally-disintegrating tablets/films per dispensing at home delivery (i.e., allow for two tablets/orally-disintegrating tablets/films per day), for 6 months:
- treatment of radiation-induced emesis,
- delayed nausea and vomiting (greater than 24 hours following chemotherapy or radiation therapy),
- as needed for nausea and vomiting after chemotherapy,
- anticipatory nausea and vomiting,
- vertigo or motion-induced nausea and vomiting,
- opioid-induced nausea and vomiting,
- treatment of postoperative nausea and vomiting,
- drug-induced (non-chemotherapy) nausea and vomiting, or
- nausea and vomiting due to other etiologies including idiopathic.

Ondansetron 4 mg/5 mL oral solution (generic only)

1. If the patient is receiving ondansetron (Zofran, generic) for the *prevention* of nausea and vomiting associated with multiple courses or multiple days of chemotherapy within 1 month, approve the quantity specified below.
- Patients ≥ 12 years of age: approve the requested quantity, not to exceed a total of 18 bottles (900 mL) per dispensing at retail or 54 bottles (2,700 mL) per dispensing at home delivery.
  Note: This override would accommodate up to 30 mL (24 mg) per day. Round up to accommodate a whole package size. For example, if the required dose is 90 mL for multiple 3-day courses of chemotherapy each on Days 1, 14, and 28 (total 270 mL), approve six 50 mL bottles (total 300 mL) per dispensing.
- Patients ≤ 11 years of age: approve the requested quantity, not to exceed a total of 9 bottles (450 mL) per dispensing at retail or 27 bottles (1,350 mL) per dispensing at home delivery.
  Note: This would accommodate a dose of 15 mL (12 mg) per day. Round up to accommodate a whole package size. For example, if the required dose is 45 mL for multiple 3-day courses of chemotherapy each on Days 1, 14, and 28 (total 135 mL), approve three 50 mL bottles (total 150 mL) per dispensing.

2. If the patient is receiving ondansetron (Zofran, generic) for the *prevention* of radiation-induced nausea and vomiting associated with multiple courses or multiple days of radiation within 1 month.
- Patients ≥ 12 years of age: approve the requested quantity, not to exceed 18 bottles (900 mL) per dispensing at retail or 54 bottls (2,700 mL) per dispensing at home delivery for 6 months.
  Note: This would accommodate a dose of 30 mL (24 mg) per day. Round up to accommodate a whole package size. For example, if the required dose is 90 mL for multiple 3-day courses of chemotherapy each on Days 1, 14, and 28 (total 270 mL), approve six 50 mL bottles (total 300 mL per dispensing).
- Patients ≤ 11 years of age: approve the requested quantity, not to exceed 9 bottles (450 mL) per dispensing at retail or 27 bottles (1,350 mL) per dispensing at home delivery for 6 months.
  Note: This would accommodates a dose of 15 mL (12 mg) per day. Round up to accommodate a whole package size. For example, if the required dose is 45 mL for multiple 3-day courses of chemotherapy each on Days 1, 14, and 28 (total 135 mL), approve three 50 mL bottles (total 150 mL per dispensing).

3. If the patient is ≥ 12 years of age AND is receiving ondansetron (Zofran, generic) for the treatment of one of the following conditions, approve the requested quantity, not to exceed 12 bottles (600 mL) per dispensing at retail or 36 bottles (1,800 mL) per dispensing at home delivery (i.e., allow for 20 mL [16 mg] per day), for 6 months:
- treatment of radiation-induced emesis
- delayed nausea and vomiting (greater than 24 hours following chemotherapy or radiation therapy),
- as needed for nausea and vomiting after chemotherapy,
- anticipatory nausea and vomiting,
- vertigo or motion-induced nausea and vomiting,
- opioid-induced nausea and vomiting,
- treatment of postoperative nausea and vomiting,
- pregnancy-induced nausea and vomiting
- drug-induced (non-chemotherapy) nausea and vomiting, or
- nausea and vomiting due to other etiologies including idiopathic.

4. If the patient is ≤ 11 years of age AND is receiving ondansetron (Zofran, generic) for the treatment of one of the following conditions, approve the requested quantity, not to exceed 6 bottles (300 mL) per dispensing at home delivery or 18 bottles (900 mL) per dispensing at home delivery (i.e., allow for 10 mL [8 mg] per day), for 6 months:
- treatment of radiation-induced emesis
- delayed nausea and vomiting (greater than 24 hours following chemotherapy or radiation therapy),
- as needed for nausea and vomiting after chemotherapy,
- anticipatory nausea and vomiting,
- vertigo or motion-induced nausea and vomiting,
- opioid-induced nausea and vomiting,
- treatment of postoperative nausea and vomiting,
- pregnancy-induced nausea and vomiting
- drug-induced (non-chemotherapy) nausea and vomiting, or
- nausea and vomiting due to other etiologies including idiopathic.

<u>Ondansetron 24 mg tablets</u>

1. If the patient is receiving ondansetron for the *prevention* of nausea and vomiting associated with multiple courses or multiple days of cancer chemotherapy within 1 month, approve the requested quantity, not to exceed 30 tablets per dispensing at retail or 90 tablets per dispensing at home delivery.

REFERENCES

1. Granisetron tablets [prescribing information]. Eatontown, NJ: West-Ward; October 2016.
2. Sancuso® transdermal system [prescribing information]. Bedminster, NJ: Kyowa Kirin; April 2020.
3. Zofran® tablets, orally disintegrating tablets, and oral solution [prescribing information]. East Hanover, NJ: Novartis; October 2021.
4. Zuplenz® oral soluble film [prescribing information]. Raleigh, NC: Aquestive; August 2021.
5. Ondansetron tablets [prescribing information]. Bachupally, India: Dr. Reddy's; May 2021