

Clinical Policy: Ondansetron (Zofran, Zuplenz)

Reference Number: CP.CPA.173

Effective Date: 11.16.16

Last Review Date: 02.19

Line of Business: Commercial

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Ondansetron (Zofran[®], Zuplenz[®]) is a serotonin (5-HT₃) receptor antagonist.

FDA Approved Indication(s)

Zofran and Zuplenz are indicated for:

- Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, including cisplatin greater than or equal to 50 mg/m²
- Prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy
- Prevention of nausea and vomiting associated with radiotherapy in patients receiving either total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen
- Prevention of postoperative nausea and/or vomiting (PONV)

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[®] that Zofran and Zuplenz are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Nausea and Vomiting (must meet all):

1. Prescribed for the prevention or treatment of nausea/vomiting due to one of the following (a, b, c, d, or e):
 - a. Cancer chemotherapy;
 - b. Radiation therapy;
 - c. Hyperemesis due to pregnancy (hyperemesis gravidarum);
 - d. Surgery;
 - e. Acute gastroenteritis in a pediatric patient;
2. Dose does not exceed one of the following (a, b, c, or d):
 - a. Chemotherapy, radiation therapy, or hyperemesis gravidarum: 24 mg per day;
 - b. Postoperative: 16 mg as a single dose;
 - c. Acute gastroenteritis: 8 mg as a single dose;
 - d. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:

Chemotherapy-induced nausea/vomiting: Projected course of chemotherapy up to 72 hours after completion of chemotherapy

Radiation therapy-induced nausea/vomiting: Projected course of radiation therapy up to 48 hours after completion of radiation therapy

Hyperemesis gravidarum: Projected duration of pregnancy

Postoperative and acute gastroenteritis nausea/vomiting: 3 days (one time dose)

B. 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.

II. Continued Therapy

A. Postoperative and Acute Gastroenteritis Nausea and Vomiting

1. Re-authorization is not permitted. Members must meet the initial approval criteria.
Approval duration: Not applicable

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, b, or c):
 - a. Continues to receive cancer chemotherapy;
 - b. Continues to receive radiation therapy;
 - c. Is pregnant;
4. If request is for a dose increase, new dose does not exceed one of the following (a or b):
 - a. Chemotherapy, radiation therapy, or hyperemesis gravidarum: 24 mg per day;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:

Chemotherapy-induced nausea/vomiting: Projected course of chemotherapy up to 72 hours after completion of chemotherapy

Radiation therapy-induced nausea/vomiting: Projected course of radiation therapy up to 48 hours after completion of radiation therapy

Hyperemesis gravidarum: Projected duration of pregnancy

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.

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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

5-HT₃: serotonin 5-hydroxytryptamine, type 3
ACOG: American College of Obstetrics and Gynecology
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

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Known hypersensitivity (e.g., anaphylaxis) to ondansetron or any components of the formulation
 - Concomitant use of apomorphine
- 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-HT₃ receptor antagonist (recommended by NCCN only). NK₁ receptor antagonists are not included in low risk antiemetic recommendations.
- Moderate emetic risk chemotherapy: 5-HT₃ receptor antagonists and dexamethasone may be used in combination and with or without NK₁ 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/m², cytarabine < 1,000 mg/m², daunorubicin, doxorubicin, epirubicin, idarubicin, ifosfamide, irinotecan, oxaliplatin
- High emetic risk chemotherapy: NK₁ receptor antagonists are recommended for use in combination with 5-HT₃ receptor antagonists and dexamethasone. Olanzapine may also be used in combination with 5-HT₃ 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-HT₃ receptor antagonists (dolasetron, ondansetron, granisetron), steroids (dexamethasone), or (haloperidol, metoclopramide, scopolamine). An NK₁ receptor antagonist may be added to the prophylaxis regimen of the next chemotherapy cycle if not previously included.

Appendix E: General Information

- The maximum injectable dose of Zofran is of 16 mg. A 32 mg single intravenous dose of Zofran (ondansetron) may affect the electrical activity of the heart (QT interval prolongation), which could pre-dispose patients to develop an abnormal and potentially fatal heart rhythm known as Torsades de Pointes.
- Micromedex has a Class IIA recommendation for oral ondansetron use for pediatric patients from 6 months to 12 years presenting with gastroenteritis.
- Use of ondansetron in pregnancy is supported in American College of Obstetrics and Gynecology (ACOG) guidelines when other agents have failed or when a patient is unresponsive to other measures and is at risk for dehydration or other adverse outcomes.

V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|--|
| Prevention of nausea and vomiting associated with cancer chemotherapy | <p>Age 6 months or older: 0.15 mg/kg IV per dose for 3 doses</p> <p>Moderately emetogenic cancer chemotherapy: <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</p> <p>Highly emetogenic cancer chemotherapy: 24 mg PO given 30 min prior to start of single-day chemotherapy</p> | <p>IV: 16 mg/dose (up to 3 doses/day) PO: 24 mg/day</p> |
| Prevention of nausea and vomiting associated with radiotherapy | <p><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</p> | 24 mg/day |

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---------------------------------|
| | <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 | |
| Prevention of postoperative nausea and vomiting | <u>Age greater than 12 years</u> : 4 mg IV as a single dose <u>Age 1 month to 12 years and more than 40 kg</u> : 4 mg IV as a single dose <u>Age 1 month to 12 years and 40 kg or less</u> : 0.1 mg/kg IV as a single dose Adults: 16 mg PO given 1 hr prior to anesthesia | IV: 4 mg/dose PO: 16 mg/dose |

VI. Product Availability

| Drug Name | Availability |
|-----------------------|---|
| Ondansetron (Zofran) | Tablets: 4 mg, 8 mg Orally disintegrating tablets (ODT): 4 mg, 8 mg Oral solution: 4 mg/5 mL Solution for injection: 40 mg/20 mL |
| Ondansetron (Zuplenz) | Oral soluble film: 4 mg, 8 mg |

VII. References

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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 |
|-------------|---|
| J2405 | Injection, ondansetron hydrochloride, per 1 mg |
| Q0162 | Ondansetron 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 48 hour dosage regimen |
| S0119 | Ondansetron, oral, 4 mg (for circumstances falling under the Medicare statute, use HCPCS Q code) |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|----------|-------------------|
| Converted to new template. Minor changes to verbiage and grammar. References updated. | 01.11.17 | 11.17 |
| 3Q 2018 annual review: modified initial and continuation approval durations for all indications; added requirement that member continue to receive chemotherapy, radiation therapy, or be pregnant for continued approval; references reviewed and updated. | 05.15.18 | 08.18 |
| 1Q 2019 annual review: no significant changes; references reviewed and updated. | 10.30.18 | 02.19 |

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.

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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.

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