09-J0000-98

Original Effective Date: 05/15/09

Reviewed: 07/10/13

Revised: 11/01/15

Subject: Ondansetron HCl (Zofran®) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

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, or transdermal route. It should be noted that oral and IV 5-HT3 antagonists have equivalent efficacy when used at the appropriate doses.

Ondansetron (Zofran) was approved by the U.S. Food and Drug Administration (FDA) in January 1991 for prevention of nausea and vomiting associated with cancer chemotherapy. Ondansetron blocks serotonin 5-HT3 receptors to prevent emesis.

In 2004, the American College of Obstetrics and Gynecology (ACOG) published an algorithm that includes ondansetron IV as a treatment option for the management of nausea and vomiting in pregnancy. There are no large trials of the effectiveness of ondansetron (or other 5-HT3 inhibitors) in nausea and vomiting in pregnancy. One small randomized controlled trial of 30 women with severe

hyperemesis gravidarum found that ondansetron was no more effective than promethazine in the management of nausea and vomiting. Additionally, there is no evidence that any one antiemetic is superior to another.

POSITION STATEMENT:

Ondansetron HCl (Zofran®) injection **meets the definition of medical necessity** for members meeting **ALL** of the following criteria:

1. Indication for use is **ONE** of the following:
    a. Prevention of chemotherapy induced nausea and vomiting
    b. Treatment of chemotherapy induced nausea and vomiting
    c. Prevention of nausea and vomiting associated with radiation treatment
    d. Prevention and treatment of post-operative nausea and vomiting
2. Member is 6 months of age or older
3. Dose does not exceed 0.15 mg/kg or 16 mg (whichever is less)

Duration of approval: 1 year

Ondansetron HCl (Zofran®) injection **meets the definition of medical necessity** for members with nausea or vomiting during pregnancy when the **ALL** of the following criteria are met:

1. Member presents with clinical signs of dehydration OR nausea and vomiting have persisted for more than 3 weeks
2. Conservative treatment has failed (e.g., dietary changes, ginger, multi-vitamin, vitamin B6 (pyridoxine) with or without doxylamine (Unisom))
3. Oral, sublingual, or rectal antiemetics have failed or are contraindicated including 4 or more of the following:
    a. Dimenhydrinate (Dramamine)
    b. Ondansetron (Zofran) or granisetron (Kytril)
    c. Promethazine (Phenergan)
    d. Trimethobenzamide (Tigan)
    e. Metoclopramide (Reglan)
4. Other injectable antiemetics have failed or are contraindicated including all of the following:
    a. Dimenhydrinate (Dramamine)
    b. Promethazine (Phenergan)
    c. Metoclopramide (Reglan)
5. Dose does not exceed 24 mg/day

Duration of approval: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 0.15 mg/kg (up to 16 mg/dose) IV approximately 30 minutes before chemotherapy; may repeat dose at 4 and 8 hours after the initial dose (dosing appropriate for adults and children age 6 months and older)
- 4 mg IV or IM prior to anesthesia induction or post-operatively (dosing appropriate for adults and children weighing greater than 40 kg)

Dose Adjustments

- Hepatic impairment (Child-Pugh score ≥ 10) – do not exceed 8 mg/day

Drug Availability

- 2 mg/mL solution for injection
- 4 mg/2 mL solution for injection

PRECAUTIONS:

Contraindications

- Hypersensitivity (e.g., anaphylaxis) to ondansetron or any of its components
- Concomitant use of apomorphine

Precautions/Warnings

- Hypersensitivity reactions including anaphylaxis and bronchospasm have been reported in individuals who have exhibited hypersensitivity to other selective 5-HT3 receptor antagonists
- QT prolongation occurs in a dose-dependent manner; avoid use in those with congenital long QT syndrome.
- Use following abdominal surgery or in those with chemotherapy-induced nausea and vomiting may mask a progressive ileus and/or gastric distention

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J2405	Injection, ondansetron hydrochloride, per 1mg

ICD-10 Diagnosis Codes That Support Medical Necessity:

021.0 – 021.9	Hyperemesis gravidarum
L59.9	Disorder of the skin and subcutaneous tissue related to radiation, unspecified

R11.0	Nausea
R11.10	Vomiting, unspecified
R11.11	Vomiting without nausea
R11.12	Projectile vomiting
R11.2	Nausea with vomiting, unspecified
T45.1x5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T50.905A	Adverse effect of unspecified drugs, medicaments and biological substances, initial encounter
T50.905S	Adverse effect of unspecified drugs, medicaments and biological substances, sequel
T66.xxxA	Radiation sickness, unspecified, initial encounter
T66.xxxS	Radiation sickness, unspecified, sequela
T88.7xxS	Unspecified adverse effect of drug or medicament, sequel
Z51.0	Encounter for antineoplastic radiation therapy
Z51.11	Encounter for antineoplastic chemotherapy

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.

DEFINITIONS:

No guideline specific definitions apply.

RELATED GUIDELINES:

Palonosetron Hydrochloride (Aloxi®), 09-J0000-87

Granisetron HCl (Kytril®) IV, 09-J0000-97

OTHER:

None applicable.

REFERENCES:

1. GlaxoSmithKline LLC. ZOFRAN (ondansetron hydrochloride) injection. 2012 [cited 2013 Jun 6]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=d9a71b42-ddfc-49d5-7280-0fc0041dba41/.
2. AHFS Drug Information. Bethesda (MD): American Society of Health-System Pharmacists, Inc; 2013 [cited 2013 Jun 6]. In: STAT!Ref Online Electronic Medical Library [Internet]. Available from: http://online.statref.com/.
3. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2013 [cited 20013 Jun 6]. Available from: http://www.clinicalpharmacology.com/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2013 Jun 6]. Available from: http://www.thomsonhc.com/.
5. NCCN Drugs & Biologics Compendium [Internet]. Fort Washington (PA): National Comprehensive Cancer Network; 2013 [cited 2013 Jun 6]. Available from: http://www.nccn.org/professionals/drug_compendium/content/contents.asp/.
6. ACOG (American College of Obstetrics and Gynecology) practice bulletin: nausea and vomiting of pregnancy. Obstet Gynecol. 2004;103:803-14.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 07/10/13.

GUIDELINE UPDATE INFORMATION:

05/15/09	New Medical Coverage Guideline.
10/15/09	Revision; consisting of clarifying dosage.
01/01/10	Revision; consisting of adding a fixed dose alternative to position statement.
08/15/10	Review and revision; consisting of updating references
01/15/11	Revision; consisting of adding ICD-10 codes.
08/15/11	Review and revision to guideline; consisting of updating position statement, dosage and administration section and references.

08/15/12	Review and revision to guideline; consisting of updating position statement, dosage maximum, precautions 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.

DECISION TREE: