

Memorandum

**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research**

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SUBJECT: One Year Post-Pediatric Exclusivity Post-marketing Adverse Event Review: Drug Use Data
Zofran[®] (ondansetron HCl): NDA 20-007, NDA 20-103, NDA 20-403, NDA 20-605, NDA 20-781
Pediatric Exclusivity Grant Date: December 1, 2004

****This document contains proprietary data which cannot be shared outside of FDA without clearance from the data vendor obtained through the Office of Drug Safety.****

EXECUTIVE SUMMARY

This consult examines drug utilization trends for oral and intravenous forms of Zofran[®] (ondansetron HCl) in the pediatric population (ages 0-16 years), with primary focus on patterns of use one year before and one year following the granting of Pediatric Exclusivity for Zofran[®] Injection, NDA 20-007, on December 1, 2004. Proprietary drug use databases licensed by the Agency were used to conduct this analysis. IMS Health, National Sales Perspective[™] was used to determine the various retail and non-retail channels of distribution. We examined the utilization patterns for Zofran[®] focusing on both the outpatient and inpatient setting. Outpatient drug use data were derived from IMS Health, National Disease and Therapeutic Index[™] (NDTI[™]), as well as from Verispan, LLC, Vector One[®]: National (VONA). Outpatient drug

utilization patterns were examined for the 3-year period from January 1, 2003, through December 31, 2005. Inpatient drug use data were derived from Premier™ Rx Market Advisor. Inpatient utilization patterns were examined for two six-month time periods, July-December 2004 and January –June 2005.

Zofran® appears to be widely used in both the outpatient and inpatient settings. In the outpatient settings, dispensed prescriptions for Zofran® to the pediatric population aged 0-16 years accounted for approximately 5.3% and 6.6% of the total prescriptions dispensed during the pre- and the post-pediatric exclusivity periods, respectively. The total number of prescriptions dispensed for Zofran® to the pediatric population aged 0-16 years increased by approximately 38.9% from the 12-month period before the pediatric exclusivity was granted (year 2004) to the following 12-month period (year 2005). In the inpatient setting, the pediatric population accounted for approximately 3% of the actual discharges associated with Zofran® during July 2004 through December 2004 and January 2005 through June 2005. The number of discharges associated with Zofran® decreased slightly when comparing the 3rd and 4th quarters of 2004 to the 1st and 2nd quarters of 2005.

OB/GYN was the most frequent prescriber specialty associated with Zofran® in 2005, accounting for approximately 23% of all dispensed prescriptions. Pediatrics accounted for approximately 4.2% of all prescriptions of Zofran® in 2005.

The most common diagnosis associated with a mention of Zofran® for patients aged 0-16 years during office-based physician-patient encounters was “malignant neoplasm of brain unspecified” (ICD-9 code 191.9), accounting for almost one-fifth of the mentions during the pre- and the post-exclusivity periods.

INTRODUCTION

On January 4, 2002, Congress enacted the Best Pharmaceuticals for Children Act (BPCA) to improve the safety and efficacy of pharmaceuticals for children. Section 17 of that Act requires the reporting of adverse events associated with the use of a drug in children during the one year following the date on which the drug received marketing exclusivity. In support of this mandate, the FDA is required to provide a report to the Pediatric Advisory Committee on the drug utilization patterns and adverse events associated with the use of the drug on a quarterly basis. This review is in addition to the routine post-marketing safety surveillance activities the FDA performs for all marketed drugs.

Zofran[®] (ondansetron HCl) Injection 2mg/ml, NDA 20-007,, a selective 5-HT₃ receptor antagonist, was approved on January 4, 1991, for the prevention nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin and for postoperative nausea and/or vomiting. Other dosage forms of Zofran[®] were approved under the following NDA's: Zofran[®] Tablets (NDA 20-103) was approved on December 31, 1992; Zofran[®] Injection Premixed 32mg/50ml (NDA 20-403) was approved on January 31, 1995; Zofran[®] Oral Solution (NDA 20-605) was approved on January 24, 1997; and Zofran[®] Orally Disintegrating Tablets (NDA 20-781) was approved on January 27, 1999.

The Pediatric Exclusivity Board of the FDA granted pediatric exclusivity for Zofran[®] (ondansetron HCl) Injection on December 1, 2004, under NDA 20-007/S-035. This review describes outpatient and inpatient drug use patterns for all forms of Zofran[®] in the pediatric and adult population in the years before and after granting the pediatric exclusivity. Proprietary drug use databases licensed by the Agency were used to conduct this analysis.

METHODS

Setting of Use

IMS Health, National Sales Perspectives[™] data (see Appendix) were used to determine the setting in which Zofran[®] was sold. Sales of this product by number of bottles of oral tablets, oral solution, and vials or premixed bags sold from the manufacturer to various retail and non-retail channels of distribution were analyzed for three 12-month time periods from January 1, 2003 through December 31, 2005. The data suggest that Zofran[®] sales in the U.S. were almost evenly distributed between retail and non-retail sales channels (data not shown). The injectable forms of this product were predominantly sold to non-federal hospitals within the non-retail channel (data not shown). Mail order pharmacies, included in the retail sales channel accounted for less than 4% of total Zofran[®] sales in 2005¹. Clinics, included in the non-retail sales channel, accounted for almost 10% of total Zofran[®] kilograms sold in 2005; however, utilization in stand-alone clinics is not captured by any database available to the Agency at this time and therefore national estimates of utilization of Zofran[®] may be underestimated.

¹ IMS Health, National Sales Perspective[™], Calendar Years 2002-2005, data extracted February, 2005; original file: 0602zof5.dvr

We examined the utilization patterns for Zofran[®] focusing on both the outpatient and inpatient settings. Outpatient drug use was derived from the IMS Health, National Disease and Therapeutic Index[™] (NDTI[™]) as well as from Verispan, LLC, Vector One[®]: National (VONA) (see Appendix). Outpatient drug utilization patterns were examined for the 3-year period from January 1, 2003 through December 31, 2005. Inpatient drug use data were derived from Premier's Rx Market Advisor and were examined for the two six-month time periods: July – December 2004 and January – June 2005. In order to put drug utilization of Zofran[®] into context, we compared drug utilization of Zofran[®] with other products from the same therapeutic class: anti-nauseants 5-HT3 receptor antagonists (USC5 17310). The drug substances in the 5-HT3 anti-nausea class included: granisetron HCl, dolasetron mesylate, dolastetron mesylate, and palonosetron HCl. Throughout our analysis, we used the agency's cut-off age definition of a pediatric patient (age 0-16 years).

RESULTS

A. Outpatient Drug Use

I. Dispensed Prescriptions

Outpatient prescriptions dispensed for anti-nausea-5-HT3 receptor antagonists (USC5 17310) as a therapeutic class increased by approximately 10% from the pre-exclusivity period (year 2004) to the post-exclusivity period (year 2005), with approximately 1.8 million prescriptions dispensed nationally in the post-exclusivity period (Table 1).

The number of outpatient prescriptions dispensed for Zofran[®] increased by approximately 11% from 1.5 million prescriptions dispensed during the pre-exclusivity period (2004) to approximately 1.6 million prescriptions dispensed during the post-exclusivity period (2005) (Table 2). Zofran[®] ranked first in this therapeutic drug class in terms of the number of prescriptions dispensed nationwide, accounting for approximately 90% of all dispensed prescriptions for the 5-HT3 anti-nausea therapeutic class as a whole. (Table 1)

Table 1. Total Number of Prescriptions Dispensed in Retail Pharmacies Nationwide for Anti-Nausea 5-HT3 Receptor Antagonists During Calendar Years 2003-2005, Verispan LLC: VONA

	2003		2004		2005	
	N*	%	N*	%	N*	%
Anti-nausea 5-HT3 Receptor Antagonists (USC5 - 17310)	1,398,000	100.0	1,607,000	100.0	1,774,000	100.0
Ondansetron (Zofran®)	1,244,000	89.0	1,459,000	90.8	1,622,000	91.5
Regular Tabs	946,000	76.0	1,006,000	68.9	1,041,000	64.2
Sublingual/Buccal Tabs	279,000	22.5	431,000	29.5	554,000	34.2
Oral Solution	12,000	1.0	16,000	1.1	18,000	1.1
Injectables	7,000	0.5	7,000	0.5	9,000	0.5
Granisetron HCl (Kytril®)	93,000	6.7	99,000	6.1	110,000	6.1
Dolasetron Mesylate (Anzemet®)	61,000	4.3	48,000	3.0	40,000	2.3
Palonosetron HCl (Aloxi®)	0	--	1,000	0.1	1,000	0.1

Verispan, LLC, 2003-2005 Data Extracted January 2005 (File: D040850 ondansetron class BPCA 1-23-06 .qry)

*Numbers rounded to thousands - Subtotals may not sum exactly due to rounding-

II. Prescriber Specialty

OB/GYN was the most frequent prescriber specialty associated with dispensed prescriptions for Zofran®, accounting for nearly one quarter of the total prescriptions dispensed during the three 12-month time period (Table 2). Oncology accounted for an estimated 9% of the dispensed prescriptions for Zofran® in 2005. Dispensed prescriptions for Zofran® prescribed by pediatricians increased the most (~48%) when comparing year 2005 to year 2004. Pediatrics accounted for approximately 4% of all dispensed prescriptions of Zofran® in 2005. The proportion of all other provider specialties prescribing Zofran® in the outpatient retail pharmacy setting showed no substantial change during the 36-month analysis period.

Table 2. Total Number of Prescriptions Dispensed for Zofran® (all forms) Nationwide by Physician Specialty During Calendar Years 2003-2005, Verispan LLC: VONA

Prescriber Specialty	2003		2004		2005	
	N *	%	N *	%	N *	%
All Prescriber Specialties	1,244,000	100.0	1,459,000	100.0	1,622,000	100.0
OB/GYN	317,000	25.5	350,000	24.0	369,000	22.8
Unspecified	143,000	11.5	185,000	12.6	180,000	11.1
Oncology	150,000	12.1	144,000	9.9	144,000	8.8
Pediatrics	36,000	2.9	46,000	3.1	68,000	4.2
Other Specialties	598,000	48.1	735,000	50.4	861,000	53.1

Verispan, LLC, 2003-2005, Data Extracted February, 2006 (File: D040850 ondansetron specialty BPCA 1-23-06.qry)

*Numbers rounded to thousands - Subtotals may not sum exactly due to rounding-

III. Patient Demographics

Prescriptions dispensed for Zofran[®] to the pediatric population aged 0-16 years increased by approximately 38.9%, from roughly 77,000 prescriptions dispensed in the pre-exclusivity period (2004) to approximately 107,000 prescriptions dispensed in the post-exclusivity period (2005) (Table 3). Dispensed prescriptions of Zofran[®] to the pediatric population aged 0-16 years accounted for approximately 5.3% and 6.6% of the total dispensed Zofran[®] prescriptions during 2004 and 2005, respectively. Dispensed prescriptions for the sublingual dosage form of Zofran[®] in the 0-16 year age group increased the most by approximately 82% from the pre- to the post-pediatric exclusivity period and accounted for approximately 50% of all total Zofran[®] prescriptions dispensed in 2005.

Table 3. Outpatient Prescriptions Dispensed for Zofran[®] by Age Groups During 2003- 2005, Verispan LLC: VONA

	2003		2004		2005	
	N*	%	N*	%	N*	%
Total	1,244,000	100.0	1,459,000	100.0	1,622,000	100.0
Age 0-16	58,000	4.7	77,000	5.3	107,000	6.6
Sublingual/Buccal Tabs	16,000	28.3	29,000	38.1	53,000	50.0
Regular Tabs	32,000	54.6	34,000	44.3	37,000	34.3
Solution	9,000	15.4	12,000	15.2	14,000	12.7
All Injectables	1,000	1.7	2,000	2.4	3,000	3.0
Age 17+	1,183,000	95.1	1,369,000	93.8	1,500,000	92.4
Unspecified	4,000	0.3	14,000	0.9	16,000	1.0

Verispan, LLC, 2003-2005, Data Extracted January 2006 (File: D040850 ondansetron age BPCA 1-23-06.qry)

* Numbers rounded to thousands - Subtotals may not sum exactly due to rounding-

According to data from Verispan's Total Patient Tracker, over the 3 years of this analysis, the estimated number of patients receiving a Zofran[®] prescription has increased approximately 41% (Table 4). The number of patients aged 0-16 years that received a ondansetron prescription has more than doubled over the three-year period.

Table 4. The Projected Number of Unique Patients Receiving a Prescription for Zofran[®] From Retail Pharmacies During Calendar Years 2003- 2005, Verispan LLC: TPT

	2003		2004		2005	
	Patient Count	%	Patient Count	%	Patient Count	%
Grand Total	604,243	100.0%	716,800	100.0%	850,131	100.0%
0 - 16	33,646	5.6%	46,329	6.5%	74,241	8.7%
17+	568,762	94.1%	663,511	92.6%	768,396	90.4%
UNKNOWN AGE	3,022	0.5%	10,361	1.4%	12,799	1.5%

Verispan, LLC Total Patient Tracker, 2003-2005, Data Extracted February 2006 (File: A060064-D040850 Zofran BPCA Custom Age Report.xls)

* Subtotals may not sum exactly due to rounding error—Row or Columns may not be added!

IV. Indications for Use

The two most common diagnoses associated with a mention of Zofran[®] for adults during office-based physician-patient encounters were “Post op surgical exam” (ICD-9 code V67.0) and “mild hyperemesis gravidarum” (ICD-9 code 643.0), accounting for approximately 28.9% and 9.2% of mentions, respectively, during the post-exclusivity period (year 2005) (Table 5). The most common diagnosis mentioned for patients aged 0-16 years old was “malignant neoplasm of brain unspecified” (ICD-9 code 191.9), accounting for approximately 19.4% and 17.7% of the mentions in the pediatric population during the pre- and the post-exclusivity time periods, respectively.

Table 5. Top Three Diagnoses Associated with Mentions of Zofran[®] for the Pediatric and Adult Population from 2003-2005, IMS Health, National Disease and Therapeutic Index[™]

IMS Reported ICD-9 Codes	2003		2004		2005	
	N*	%	N	%	N	%
Zofran[®] Total Mentions	1,534,000	100.0	1,411,000	100.0	1,857,000	100.0
Age 17+ Years	1,374,000	89.6	1,253,000	88.8	1,684,000	90.7
V67.0 Post op surgical exam	382,000	27.8	410,000	32.7	487,000	28.9
643.0 Mild hyperemesis gravidarum	109,000	8.0	65,000	5.2	154,000	9.2
787.0 Nausea and vomiting	51,000	3.7	79,000	6.3	86,000	5.1
Other Diagnoses (166)	756,000	55	605,000	48.3	834,000	49.5
Age 1-16 Years	112,000	7.3	132,000	19.4	113,000	6.1
191.9 Malignant neoplasm of brain unspecified	18,000	15.9	26,000	19.4	20,000	17.7
008.8 Other organism not classified	-----		-----		-----	
09.1 Colitis, enteritis, gastroenteritis of presumed infectious origin	4,000	3.8	14,000	10.8	11,000	9.5
Other Diagnoses (36)	90,000	80.3	92,000	69.8	67,000	59.3
Unspecified	48,000	3.1	26,000	1.8	60,000	3.2

IMS Health, National Disease and Therapeutic Index[™] CD-ROM, NDTI 3 year. January 2003-December 2005. Data extracted February 2006 (File: zofranbyagedig4.dvf)

*rounded to thousands

B. Inpatient Drug Usage

Utilizing Premier’s database of 450 acute care hospitals, there were 400,213 actual discharges associated with a charge for any dosage form of Zofran[®] during the 6 months prior to the granting of exclusivity (July 2004 – December 2004) and 389,230 discharges in the 6 months following the granting of exclusivity (January 2005 – June 2005) (Table 6). This represents a

2.7% relative decrease in the discharges associated with Zofran[®] use from the pre- to the post-exclusivity period. Pediatric patients ages 0 – 16 years accounted for 13,171 discharges (3.3%) in the pre-exclusivity period and for 12,393 discharges (3.2%) in the post-exclusivity period, a 7.3% decrease. Patients ages 0-1 years old accounted for 35.9% increase in the discharges associated with a Zofran[®] charge, increasing from 883 actual discharges (6.7%) in the pre-exclusivity period to 1,200 actual discharges (9.7%) in the post-exclusivity period.

Table 6. Acute Care Hospital Discharges Associated with a Charge for Zofran[®] (ondansetron) for the 6 months before and after exclusivity, Premier[™] (July 2004 – June 2005)

	July 1 - December 31 2004		January 1 - June 30 2005	
	Number of Actual Discharges			
	N [†] (%)		N (%)	
Total	400,213	100.0	389,230	100.0
Age 0-16	13,371	3.3	12,393	3.2
Age 0-1	883	6.7	1,200	9.7
Age 2-11	5,996	45.5	5,618	45.3
Age 12-16	6,292	47.8	5,575	45.0
Age 17+	387,042	96.7	376,837	96.8

Source: Premier Informatics Extracted 2-2-06 file
(Zofran BPCA.xls)

[†]Subtotals may not sum correctly due to rounding

In a subset of 37 Premier Network pediatric hospitals and care centers, discharges associated with a charge for any Zofran[®] for patients aged 0-16 years declined by 12% from 6,784 discharges during the 6 months prior to the granting of exclusivity (July 2004 – December 2004) to 5,970 discharges during the 6 months after the granting of exclusivity (January 2005 – June 2005) (Table 7).

Table 7. Pediatric Care Center Discharges Associated with a Charge for Zofran[®] (ondansetron) for the 6 months before and after exclusivity, Premier[™] (July 2004 – June 2005)

	July 1 - December 31 2004		January 1 - June 30 2005	
	Number of Actual Discharges			
	N	(%)	N	(%)
Age 0-16	6,784	100.0	5,970	100.0
<i>Age 0-1</i>	555	8.2	605	9.0
<i>Age 2-11</i>	3,509	51.7	3,111	52.1
<i>Age 12-16</i>	2,720	40.1	2,254	37.8

Source: Premier Informatics Extracted 2-2-06 file
(Zofran BPCA peds hosp.xls)

[†]Subtotals may not sum correctly due to rounding

DISCUSSION

Based on the databases used for this consult, the use of 5-HT₃ receptor antagonists increased during the three 12-month periods from 2003 to 2005. Total dispensed prescriptions for 5-HT₃ receptor antagonists and specifically Zofran[®] has been increasing from the pre- to the post-exclusivity periods. 5-HT₃ receptor antagonists, and predominantly Zofran[®], are widely used in adults and children in the prophylactic treatment of chemotherapy-induced nausea and vomiting or prophylaxis of postoperative vomiting. The use of Zofran[®] in the pediatric population aged 0-16 years appears to be increasing, yet the majority of use of this product was in adults.

Surprisingly, we found that over one-fifth of the prescriptions dispensed for Zofran[®] are prescribed by OB/GYN specialty. Since pregnant women often experience nausea and vomiting primarily during the first trimester, this finding may suggest that Zofran[®] (pregnancy category B) may have been prescribed to pregnant women for mild hyperemesis gravidarum (HG), even though it is not indicated for this use. Few cases have been reported in the medical literature on the use of Zofran[®] to treat HG, which may be as frequent as one in 200 pregnant women.¹⁻³ Unlike common nausea and vomiting, HG may have negative implications for maternal and fetal health that may result in the need for pharmacologic therapy. Although Zofran[®] appears to be beneficial and does not appear to be associated with an increased risk of malformation above baseline, safety data are limited.^{4,5}

Findings from this consult should be interpreted in the context of the known limitations of the databases used. We estimated that the use of Zofran[®] was mostly in the outpatient settings based on IMS Health, National Sales Perspectives[™] data. These data do not provide a direct estimate of use but do provide a national estimate of units sold from the manufacturer to various channels of distribution. The amount of product purchased by these retail and non-retail channels of

distribution may be a possible surrogate for use, if we assume that facilities purchase drugs in quantities reflective of actual patient use.

NDTI™ data provide estimates of patient demographics and indications for use of medicinal products in the U.S. Due to the sampling and data collection methodologies, the small sample size can make these data unstable, particularly when use is not common in the pediatric population.

CONCLUSION

In summary, Zofran® usage in the pediatric and adult population has increased over the past three years. Dispensed prescriptions for Zofran® for pediatric patients aged 0-16 years increased by nearly 39% from the pre-exclusivity period (year 2004) to the post-exclusivity period (year 2005). Pediatric patients aged 0-16 accounted for approximately 6.6% of the total dispensed prescriptions in year 2005 with the sublingual dosage form most commonly prescribed to this age group. Prescriptions written by pediatricians increased by almost 48% from the pre-exclusivity period (year 2004) to the post-exclusivity period (year 2005).

APPENDIX

IMS HEALTH, IMS NATIONAL SALES PERSPECTIVES™

IMS Health National Sales Perspectives™ measures the volume of drug products (both prescription and over-the-counter) and selected diagnostic products moving from manufacturers into various outlets within the retail and non-retail markets in terms of sales dollars, vials, and market share. Outlets within the retail market include the following pharmacy settings: chain drug stores, independent drug stores, mass merchandisers, food stores, and mail service. Outlets within the non-retail market include clinics, non-federal hospitals, federal facilities, HMOs, long-term care facilities, home health care, and other miscellaneous settings. These data are projected nationally to reflect national drug sales patterns.

For this analysis, the sales trends of Zofran® were examined from January 1, 2003 – December 31, 2005 inclusive.

VERISPAN, LLC

Vector One®: National (VONA)

Verispan's VONA measures retail dispensing of prescriptions or the frequency with which drugs move out of retail pharmacies into the hands of consumers via formal prescriptions. Information on the physician specialty, the patient's age and gender, and estimates for the numbers of patients that are continuing or new to therapy are available.

The Vector One® database integrates prescription activity from a variety of sources including national retail chains, mass merchandisers, pharmacy benefits managers and their data systems, and provider groups. Vector One® receives over 1.8 billion prescription claims, representing over 150 million unique patients.

The number of dispensed prescriptions is obtained from a sample of virtually all retail pharmacies throughout the U.S and represents approximately half of the retail prescriptions dispensed nationwide. Verispan receives all prescriptions from approximately one-third of the stores and a significant sample of prescriptions from the remaining stores.

Data for this analysis included prescriptions dispensed for 5-HT3 receptor antagonists including Zofran® from January 1, 2003 – December 31, 2005 inclusive.

VERISPAN, LLC

Vector One®: Total Patient Tracker (TPT)

Verispan's Total Patient Tracker is a national-level projected audit designed to estimate the total number of unique patients across all drugs and therapeutic classes.

TPT derives its data from the Vector One® database which integrates prescription activity from a variety of sources including national retail chains, mass merchandisers, pharmacy benefits

managers and their data systems, physician offices and hospitals. Vector One[®] receives over 1.8 billion prescription claims per year, which represents over 150 million patients tracked across time.

Data for this analysis included patients who were dispensed prescriptions for Zofran[®] from January 1, 2003 – December 31, 2005 inclusive.

IMS HEALTH, NATIONAL DISEASE AND THERAPEUTIC INDEX™ (NDTI™)

The National Disease and Therapeutic Index™ (NDTI™) is an ongoing survey designed and conducted by IMS Health to provide descriptive information on the patterns and treatment of diseases encountered in office-based practices in the continental U.S. The data are collected from a panel of approximately 3,000 office-based physicians who complete and submit a survey of their practice patterns to IMS Health for two consecutive days per quarter. These data may include profiles and trends of diagnoses, patients, drug products mentioned, and treatment patterns. These data are projected nationally to reflect national prescribing patterns.

NDTI™ uses the term drug uses for mentions of a drug in association with a diagnosis during an office-based patient visit. This term may be duplicated by the number of diagnosis for which the drug is mentioned. It is important to note that a drug use does not necessarily result in prescription being generated. Rather, the term indicates that a given drug was mentioned during an office visit.

For this analysis, we examined annual mentions of Zofran[®] during office-based physician visits during the time period from January 1, 2003 – December 31, 2005 inclusive.

PREMIER (RX MARKET ADVISOR)

Premier's database is a large hospital drug utilization and financial database. The data are derived from over 450 acute care facilities and include approximately 18 million inpatient records. On an annual basis, this constitutes roughly one out of every seven inpatient discharges in the United States. Data are available from January 2000 through the present, but have a lag time of approximately six months. Premier's primary mission is to assist health care institutions improve clinical and operating performance in three strategic areas: group purchasing, supply chain and healthcare informatics. To that end, the Premier Informatics group developed this database in part to analyze utilization of resources to improve clinical efficiency.

Hospitals that contribute information to this database are a select sample of both Premier and U.S. institutions, and do not necessarily represent all hospitals in the U.S. Data are collected from this sample of participating hospitals with diverse characteristics based upon geographic location, bed size, population served, payors and teaching status. The data collected include demographic and pharmacy-billing information, as well as all diagnoses and procedures for every patient discharge. Preliminary comparisons between participating Premier hospital and patient characteristics and those of the probability sample of hospitals and patients selected for the National Hospital Discharge Survey (NHDS) appeared to be very similar with regard to

patient age, gender, length of stay, mortality, primary discharge diagnosis and primary procedure groups.

For this analysis, we examined inpatient discharges associated with Zofran[®] during the two six month time periods from July 1 – December 31, 2004 and January 1 – June 30, 2005, inclusive.

PREMIER PEDIATRIC™

Premier's pediatric database represents a subset of information from 37 pediatric hospitals. In addition, Premier maintains data on all pediatric discharges from the larger sample of approximately 450 acute care facilities. Overall, the pediatric population in Premier's pediatric database includes greater than 3 million inpatient records. Data are available from January 2000 through the present, but have a lag time of approximately six months.

For this analysis, the total number of distinct discharges associated with Zofran[®] use within these 37 tertiary care pediatric hospitals was examined for the 6 months before and after the granting of exclusivity; a one year time period from July 1, 2004 –June 30, 2005, inclusive.

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Concurrences:

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