

MEMORANDUM

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

PID#: D040224

DATE: June 15, 2005

FROM: Kendra Worthy, Pharm.D.
Pharmacist/Drug Use Specialist
Division of Surveillance, Research and Communication Support, HFD-410

Judy Staffa, Ph.D, R.Ph.
Epidemiologist Team Leader
Division of Surveillance, Research and Communication Support, HFD-410

THROUGH: Gerald DalPan, M.D., Director
Division of Surveillance, Research and Communication Support, HFD-410

TO: Solomon Iyasu, MD, MPH
Div. of Pediatric Drugs and Development, HFD-960
Office of Counter-Terrorism and Pediatric Development

SUBJECT: One Year Post-Pediatric Exclusivity Postmarketing Adverse Event Review: Drug Use Data
Irinotecan (Camptosar®, NDA 20-571)
Pediatric Exclusivity Grant Date: March 10, 2004

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

EXECUTIVE SUMMARY

This consult examines the drug use for Camptosar® (irinotecan) in the pediatric population (0-16 years), with primary focus on patterns of use one year before and one year following the granting of Pediatric Exclusivity on March 10, 2004. Proprietary drug use databases licensed by the Agency were used to conduct this analysis. The IMS Health IMS National Sales Perspectives™ was used to determine the various retail and non-retail channels of distribution. The estimated sale of irinotecan has remained consistent from 2002 to 2004, with just over 1 million vials sold in each year. It was clear from these data that the majority of this product was sold into non-retail settings; 98.7% of all vials sold were to non-retail pharmacies during year 2004, of which

70% was sold to clinics. Since the Agency does not have access to data describing the use of drug products in clinics, we could only examine the utilization patterns for irinotecan focusing on the inpatient setting. Inpatient use was assessed from hospital billing data provided by Premier™. *It should be noted, however, that the inpatient use described in the current analysis likely reflects only 25% of the total use of irinotecan.*

Overall, the inpatient use of irinotecan appears to have remained steady over the two year study period from October 1, 2002 to September 31, 2004. Use of irinotecan is primarily in the adult population. “Chemotherapy” (ICD-9 V58.1) was the most common procedural diagnosis for children that was associated with discharges in which irinotecan was billed. Pediatric use represented approximately 16% of actual discharges in which irinotecan was billed among Premier’s 450 acute-care facilities during the 2-year time period.

A major limitation of the current analysis is that the data resources available to the Agency do not capture use of irinotecan in the outpatient clinic setting, which represents approximately 75% of its use.

INTRODUCTION

On January 3, 2001, Congress enacted the Best Pharmaceuticals for Children Act (BPCA) to improve the safety and efficacy of pharmaceuticals for children. Section 17 of the BPCA requires the reporting of adverse events associated with the use of a drug in children during the one-year period following the date on which the drug received pediatric 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.

Camptosar® (irinotecan injection 20 mg/mL) NDA 20-571 is an antineoplastic agent of the topoisomerase I inhibitor class. It is indicated as a component of first-line therapy in combination with 5-fluorouracil and leucovorin for patients with metastatic carcinoma of the colon or rectum. It is also used for the treatment of patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed following 5-FU-based therapy.

Camptosar® was approved on June 14, 1996, and is available for intravenous injection in 2 and 5 mL single-dose vials. The Pediatric Exclusivity Board of the FDA granted pediatric exclusivity for Camptosar® Injection (NDA 20-571) on March 10, 2004.

This review describes only inpatient drug use patterns for Camptosar® in the pediatric population as well as in the adult population in the years prior to and subsequent to the granting of pediatric exclusivity. Proprietary drug use databases licensed by the Agency were used to conduct this analysis.

METHODS

A. Determining Setting of Use

IMS Health, IMS National Sales Perspectives™ data (see Appendix for details on this data resource) were used to determine the setting in which the product was sold. Sales of this product by number of vials sold from the manufacturer to various retail and non-retail channels of distribution were analyzed for March 2003 through April 2004. The estimated sale of irinotecan has remained consistent from 2002 to 2004, with just over 1 million vials sold in each year. It was clear from these data that the majority of this product was sold into non-retail settings; 98.7% of all vials sold were to non-retail pharmacies during year 2004, of which 70% were sold to clinics. Since the Agency does not have access to data describing the use of drug products in clinics, we could only examine the utilization patterns for irinotecan focusing on the inpatient setting. Inpatient use was assessed from hospital billing data provided by Premier™. *It should be noted, however, that the inpatient use described in the current study likely reflects only a quarter of the total use of irinotecan.*

B. Data Resources

For this analysis, the total number of projected discharges associated with irinotecan within Premier hospitals was examined for the time period from October 1, 2002 to September 30, 2004, inclusive. Irinotecan use was also examined within a subgroup of 37 children's hospitals in the Premier database using the same time window (see Appendix for details on this data resource).

RESULTS

A. Acute, short-stay hospitals

Acute Care Hospitals

Overall, the inpatient use of irinotecan appears to be fairly stable over the two year study period from October 1, 2002 to September 30, 2004. Inpatient use of irinotecan is primarily in the adult population. “Chemotherapy” (ICD-9 V58.1) was the most common procedural diagnosis for children that was associated with discharges in which irinotecan was billed. Pediatric use represented approximately 16% of actual discharges in which irinotecan was billed among Premier’s 450 acute-care facilities during both time periods.

Table 1: Total Number of Actual Discharges Associated with Irinotecan by Age Groups in Premier Hospitals, October 2002 through September 2004 (Rx Market Advisor™)

Patient Age Custom Groups	ICD-9	Principal Diagnosis	October 2002 - September 2003	October 2003 - September 2004
			Actual Discharges	Actual Discharges
Total			652	596
Patient Age 0-16	Total		108	97
Patient Age 0-16	V58.1	Chemotherapy	105	97
Patient Age 0-16	V30.0	Single Liveborn Hosp w/o C-Sec	3	0
Patient Age 17 and Above	Total		544	499
Patient Age 17 and Above	151.2-162.9	Malignant Neoplasms	117	84
Patient Age 17 and Above	197-198.89	Secondary Malig. Neoplasms	121	104
Patient Age 17 and Above		All other ICD-9 (8)	306	311

Premier Rx Market Advisor, data extracted April 2005.

B. Pediatric Hospitals

In the subset of 37 pediatric hospitals, there was a total of 42 discharges associated with the use of irinotecan in the pediatric population (ages 0-16) during the two-year time period (Table 2).

DISCUSSION

Table 2: Total Number of Actual Discharges Associated with Irinotecan by Age in Premier Pediatric Hospitals, October 2002 through September 2004 (Rx Market Advisor™)

				October 2002 - September 2003	October 2003 - September 2004
Total Irinotecan	Age	ICD-9	Principal Diagnosis	Discharges	Discharges
			Single Liveborn-Hosp w/o C- Sec	3	0
	0	V30.0			
	2	V58.1	Chemotherapy	0	6
	3	V58.1	Chemotherapy	6	3
	4	V58.1	Chemotherapy	3	0
	9	V58.1	Chemotherapy	6	6
	11	V58.1	Chemotherapy	0	3
	13	V58.1	Chemotherapy	3	0
	15	V58.1	Chemotherapy	3	0
Total Irinotecan				24	18

Premier Pediatric Rx Market Advisor, data extracted April 2005.

Based on sales data and data reflecting inpatient use, it appears that the use of irinotecan has remained consistent over the past three years, 2002 to 2004. A major limitation of the current analysis is that the data resources available to the Agency do not capture use of irinotecan in the outpatient clinic setting, which represents approximately 75% of its use.

The limitations of sales data should be borne in mind when considering this analysis. The IMS Health, IMS National Sales Perspectives™ does not provide a direct estimate of use but does provide a national estimate of units sold from the manufacturer to various channels of distribution. It does not include demographic information for the patients receiving these products, such as age and gender. 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.

Inpatient data also have limitations to consider when interpreting use estimates. Premier data are derived from hospital billing data, and therefore may not reflect exactly what drugs are administered to patients. Also, there are no direct linkages between billed drugs and discharge

diagnoses and procedures, so indications for use cannot be determined. Finally, we are not able to use Premier data to make reliable national estimates of drug use for the subpopulation of pediatric inpatients at this time. Although Premier hospitals appear representative of all U.S. acute short-stay hospitals in general, it is not clear whether they are representative of pediatric inpatient care in the U.S.

CONCLUSION

Sales of irinotecan have remained steady from March 2002 to April 2004, with just over 1 million vials sold each year. Approximately 25% of irinotecan is used in the inpatient setting, and its use appears to have remained relatively steady over the two year study period from October 1, 2002 to September 30, 2004. Use of irinotecan is primarily in the adult population. In children (ages 0-16 years), “chemotherapy” (ICD-9 V58.1) was the most common procedural diagnosis associated with the discharges in which irinotecan was billed. Pediatric discharges represented approximately 16% of actual discharges in which irinotecan was billed among Premier’s 450 acute-care facilities during the 2-year time period.

A major limitation of the current analysis is that the data resources available to the Agency do not capture use of irinotecan in the outpatient clinic setting, which represents approximately 75% of its use.

APPENDIX

IMS HEALTH, IMS NATIONAL SALES PERSPECTIVES™

IMS Health IMS 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. 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. IMS Health, National Sales Perspectives™ measures the volume of drug products moving from manufacturer into retail and non-retail settings in terms of sales dollars, vials, and market share. These data are based on national projections.

PREMIER™

Premier maintains a large hospital drug utilization and financial database which contains billing information from over 450 acute care facilities and includes approximately 14 million inpatient records. Roughly one out of every seven inpatient discharges in the United States is represented in Premier's database. Data are available from January 2000 through the present, but have a lag time of approximately 6 months.

The 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, number of beds, 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) proved to be very similar with regard to patient age, gender, length of stay, mortality, primary discharge diagnosis and primary procedure groups. Based upon these analyses, we believe that overall estimates of national inpatient drug use using Premier data appear to be reasonable, but strongly recommend making this determination on a drug-specific and population-specific basis. We used only actual sample estimates for irinotecan, since we cannot use Premier data at this time to make reliable national estimates of drug use for the subpopulation of pediatric inpatients.

PREMIER PEDIATRIC™

Premier's pediatric database is a subset of the larger database described above. Information is available from 37 pediatric hospitals. Data are also available from January 2000 through the present, but have a lag time of approximately six months.

Kendra Worthy, Pharm.D.
**Pharmacist/Drug Utilization Data
Specialist**
**Division of Surveillance, Research, and
Communication Support (DSRCS)**

Judy Staffa, Ph.D., R.Ph.
Epidemiologist
Team Leader
**Division of Surveillance, Research, and
Communication Support (DSRCS)**

Laura A. Governale, Pharm.D., MBA
**Pharmacist/Drug Utilization Data
Specialist, Team Leader**
**Division of Surveillance, Research, and
Communication Support (DSRCS)**

Gerald Dal Pan, M.D., MHS
Division Director
**Division of Surveillance, Research, and
Communication Support (DSRCS)**