

**Memorandum**

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

**PID#:** A060340  
**DATE:** August 30, 2006  
**FROM:** Laura A. Governale, Pharm.D., MBA / Drug Use Data Specialist Team Leader  
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**THROUGH:** Solomon Iyasu, MD, MPH, Director  
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**TO:** Carolyn Yancy MD, Medical Officer  
Division of Anesthesia, Analgesia, and Rheumatology Products  
**SUBJECT:** Pediatric drug use review for Celebrex<sup>®</sup> (celecoxib); NDA 20-998/S-021

**\*\*This document contains proprietary drug use data obtained by FDA under contract. The drug use data/information cannot be released to the public/non-FDA personnel without contractor approval obtained through the FDA/CDER Office of Surveillance and Epidemiology.\*\***

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**Background:**

In response to a request for drug use data by the Division of Anesthesia, Analgesia, and Rheumatology Products (DAARP), this consult examines the utilization of Celebrex<sup>®</sup> (celecoxib), NDA 20-998, in the pediatric population, ages 0-18 years.

Celebrex<sup>®</sup> is currently not indicated for use in the pediatric population. DAARP has requested this consult in preparation for an upcoming Advisory Committee meeting on November 29, 2006, to discuss the efficacy supplement for Celebrex<sup>®</sup> (celecoxib), NDA 20-998/S-021, in the pediatric population, ages 2-18 years, for the treatment of Juvenile Rheumatoid Arthritis (JRA). Currently, Celebrex<sup>®</sup> has the following indications:

1. For relief of the signs and symptoms of osteoarthritis.
2. For relief of the signs and symptoms of rheumatoid arthritis in adults.
3. For the relief of signs and symptoms of ankylosing spondylitis.
4. For the management of acute pain in adults.
5. For the treatment of primary dysmenorrhea.
6. To reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis (FAP), as an adjunct to usual care (e.g., endoscopic surveillance, surgery).

This consult provides analyses of the distribution channels for Celebrex<sup>®</sup>, the numbers of prescriptions dispensed (by patient age and by prescribing physician specialty) and the number of unique patients who have received a prescription for Celebrex<sup>®</sup> from retail pharmacies from year 2002 through June 2006.

## Memo:

### Wholesale Sales Distribution

The IMS Health, IMS National Sales Perspectives™ measures the distribution of pharmaceutical products from manufacturers into the retail and non-retail markets. The majority of sales for Celebrex® (celecoxib) was distributed to retail channels which accounted for approximately 65% of the estimated 674 million capsules of product sold during July 2005 – June 2006<sup>1</sup>. The retail channels include chain pharmacies, independents, food stores with pharmacies, and mass merchandisers with pharmacies. The mail service channel accounted for approximately 26% of sales distribution and the non-retail channels accounted for approximately 9% of sales distribution.

### Outpatient Dispensing Volume and Patient Demographics

#### Outpatient Dispensing: Prescription Counts and Physician Specialty

Verispan's VONA measures nationally projected outpatient prescriptions dispensed through retail pharmacies, excluding mail order pharmacies. Since year 2002, the number of dispensed prescriptions for pediatric patients has decrease by almost two-thirds from 112,000 (95% CI 111,000-113,000) prescriptions to 41,000 (95% CI 40,500 – 41,500) prescriptions by year 2005 (Table 1). The most dramatic decline in use was noted between year 2004 and 2005 where the number of dispensed prescriptions decreased by half from 80,000 (95% CI 79,400 – 80,600) to 41,000 (95% CI 40,500 – 41,500). Similar decline in use were observed for adults. Throughout this time period, less than 1% of all dispensed prescriptions for Celebrex® were for pediatric patients age 0-18 years.

Table 1. Total Retail Prescriptions Dispensed (in thousands) for Celebrex® by Age (0-18, 19+) From Year 2002 – June 2006.

	2002		2003		2004		2005		Jan-Jun 2006	
	TRxs (000)	Share %								
<b>Celebrex® (celecoxib)</b>	21,234	100.0%	18,882	100.0%	19,038	100.0%	10,965	100.0%	5,520	100.0%
<b>0-18</b>	112	0.5%	88	0.5%	80	0.4%	41	0.4%	20	0.4%
<b>19+</b>	21,032	99.0%	18,704	99.1%	18,806	98.8%	10,825	98.7%	5,482	99.3%
<b>UNSPEC.</b>	90	0.4%	90	0.5%	152	0.8%	99	0.9%	19	0.3%

Verispan Vector One® : National, Years 2002 – June 2006, Extracted 8-25-2006; VONA Governale 8-25-06 A060304 Celebrex PdIT TRxAg.xls

<sup>1</sup> IMS Health, IMS National Sales Perspectives™, July 2005 – June 2006, Extracted 8-25-06. Original file: 0608cele.dvr

## Physician Specialty

General Practice specialty was the most common physician specialty associated with a dispensed prescription for Celebrex<sup>®</sup>, accounting for approximately 30% of dispensing during the entire study period (Table 2). The Internal Medicine specialty was next in ranking and accounted for over 25% of dispensed prescriptions. Pediatricians ranked 13<sup>th</sup> in relation to all other specialties, accounting for less than 1% of all prescriptions dispensed for Celebrex<sup>®</sup> from year 2002 through June 2006.

Table 2. Total Retail Prescriptions Dispensed for Celebrex<sup>®</sup> (celecoxib) in Thousands by Physician Specialty, from Year 2002 to June 2006.

	2002		2003		2004		2005		Jan-Jun 2006	
	TRxs (000)	Share	TRxs (000)	Share %	TRxs (000)	Share %	TRxs (000)	Share %	TRxs (000)	Share %
<b>Celecoxib</b>	21,234	100.0%	18,882	100.0%	19,038	100.0%	10,965	100.0%	5,520	100.0%
1 <b>General practice*</b>	6,654	31.3%	6,030	31.9%	6,009	31.6%	3,720	33.9%	1,919	34.8%
2 <b>IM</b>	5,337	25.1%	4,905	26.0%	4,898	25.7%	2,790	25.4%	1,407	25.5%
3 <b>ORTH SURG</b>	2,078	9.8%	1,699	9.0%	1,613	8.5%	913	8.3%	513	9.3%
4 <b>RHEUM</b>	1,058	5.0%	890	4.7%	843	4.4%	599	5.5%	309	5.6%
5 <b>UNSPEC</b>	2,005	9.4%	1,617	8.6%	1,933	10.2%	882	8.0%	246	4.5%
... <b>All Others</b>	3,932	18.5%	3,583	19.0%	3,577	18.8%	1,969	18.0%	1,077	19.5%
13 <b>PED</b>	171	0.8%	161	0.9%	165	0.9%	92	0.8%	48	0.9%

\*General Practice includes general practice, Family Medicine, Doctors of Osteopathy

Verispan Vector One<sup>®</sup> : National, Years 2002 – June 2006, Extracted 8-25-2006; VONA Governale 8-25-06 A060304 Celebrex PdIT MD.xls

When we looked at drug use mentions as reported by office-based physician practices, the majority of drug occurrences for Celebrex<sup>®</sup> in the pediatric population (age 0-18) were reported by the Orthopedic Surgery specialty, which accounted for approximately 66% of drug occurrences for the combined time period of year 2002 through June 2006 (Table 3). Drug occurrences reported by Rheumatologists accounted for less than 10% of mentions for the pediatric population during this time period.

Table 3. Total Number of Drug Occurrences as Reported by Office-Based Physician Practices for Celebrex<sup>®</sup> from Years 2002 through June 2006 Combined.

Celebrex <sup>®</sup>	Drug Occurrences (000)	Share %
<b>Patient Age 0-18</b>	1,266	100.0%
<b>ORTH SURG</b>	842	66.5%
<b>GP/FM/DO</b>	172	13.6%
<b>RHEUM</b>	116	9.2%
<b>POD</b>	35	2.8%
<b>EM</b>	10	0.8%
<b>PED</b>	33	2.6%
<b>OB/GYN</b>	16	1.3%
<b>IM</b>	21	1.7%
<b>ENT</b>	3	0.2%
<b>UROL</b>	6	0.5%
<b>GEN SURG</b>	6	0.5%
<b>AO SURG</b>	6	0.5%

Outpatient Dispensing: Patient Counts

Verispan’s Total Patient Tracker (TPT) is a national-level projected audit designed to estimate the total number of unique patients receiving prescriptions dispensed through outpatient retail pharmacies. Patient counts were obtained from year 2002 to June 2006 for the dispensing of Celebrex<sup>®</sup>. The proportion of patients in each age band (Table 4) is similar to the proportions of prescriptions in each age band (Table 1). Pediatric patients accounted for 1% or less than 1% of all patients who received a prescription for Celebrex<sup>®</sup>. Similar to dispensed prescription data, the number of patients receiving a prescription for Celebrex<sup>®</sup> also decreased dramatically between year 2004 and 2005.

Table 4: Patients Receiving a Prescription for Celebrex<sup>®</sup> (celecoxib) from Outpatient Retail Pharmacies by Patient Age, Years 2002 - June 2006.

	Year 2002		Year 2003		Year 2004		Year 2005		Jan-Jun 2006	
	Projected Patient Count	Total Patient Share								
Product Total	<b>6,632,610</b>		<b>5,966,299</b>		<b>5,966,074</b>		<b>3,214,208</b>		<b>2,228,823</b>	
0 – 18 Years	68,302	1.03%	54,480	0.91%	52,227	0.88%	22,436	0.70%	12,481	0.56%
19+ Years	6,552,694	98.80%	5,868,901	98.37%	5,834,131	97.79%	3,150,827	98.03%	2,208,836	99.10%
Unknown Age	54,099	0.82%	110,446	1.85%	164,236	2.75%	91,309	2.84%	19,770	88.80%

Verispan Vector One: Total Patient Tracker (TPT) Data Extracted 8-2006; TPT A060340 8-23-06 COX2s.xls,

\*Due to aging of patients during the study period (“the cohort effect”), patients may be counted more than once in the individual age categories. For this reason, summing across age bands is not advisable and will result in overestimates of patient counts.

\*\*Subtotals may not sum exactly, due to rounding error.

Indications for use

Verispan’s PDDA is a national survey which measures the indication for use of drug products mentioned during patient visits to office based physicians. Sprains of ankle and foot (ICD-9 845), and Osteocondropathies (ICD-9 732) were the two most commonly mentioned diagnoses associated with Celebrex<sup>®</sup> in the pediatric population during year 2004 and 2005<sup>2</sup>. Due to the survey’s small sample size and the relatively low usage of Celebrex<sup>®</sup> in this population, a consistent trend could not be identified for any specific diagnosis during this analysis period. However, when all sprain injuries were combined, the totality of sprain injuries appeared to be the most common grouped diagnosis for the entire analysis period<sup>†</sup>.

**Conclusion**

Less than 1% of total dispensed prescriptions for Celebrex<sup>®</sup> are for the pediatric population, ages 0-18, during years 2002 through June 2006. Similarly, the number of pediatric patients receiving a prescription for Celebrex<sup>®</sup> were less than 1% of the total during this time period. According to dispensed prescriptions, the majority of prescribing for Celebrex<sup>®</sup> were by General Practice and Internal Medicine specialties. According to office-based physician surveys, Orthopedic Surgeons appear to be the most common prescriber for Celebrex<sup>®</sup> to the pediatric population. The most common diagnoses associated with Celebrex<sup>®</sup> are for sprains and injuries.

<sup>2</sup> Verispan, PDDA, Years 2002 – June 2006, Extracted 8-25-06; PDDA A060340 8-25-06 Celebrex AgDx3.xls.

<sup>†</sup> Sprain of ankle and foot (ICD-9 845) and Spring of knee and leg (ICD-9 844) combined

## DATA SOURCES

This review describes the annual sales and drug use patterns of Dovonex<sup>®</sup> with an emphasis on use in the pediatric population (ages 0 through 17 years). Proprietary drug use databases licensed by the Agency were used to conduct this analysis. The data sources for this analysis are described in detail below.

### *Outpatient Drug Usage*

#### **IMS HEALTH**

IMS National Sales Perspectives<sup>™</sup>

IMS Health National Sales Perspectives<sup>™</sup> measures the volume of drug products (both prescription and over-the-counter) and selected diagnostic products moving from manufacturers into retail and non-retail markets. The volume of drug products transferred to these markets is expressed 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 based on national projections.

#### **VERISPAN, LLC**

Vector One<sup>®</sup>: National (VONA)

Verispan's VONA is a nationally projected database which measures the 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<sup>®</sup> 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<sup>®</sup> receives over 2 billion prescription claims yearly, representing over 160 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. Mail order prescriptions are not included in the sample at this time.

#### **VERISPAN, LLC**

Vector One<sup>®</sup>: 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<sup>®</sup> 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<sup>®</sup> receives over 2 billion prescription claims per year, which represents over 160 million unique patients tracked across time.

#### **VERISPAN, LLC**

Physician Drug & Diagnosis Audit (PDDA)

Verispan's Physician Drug & Diagnosis Audit (PDDA) is a monthly survey that monitors disease states and the physician intended prescribing habits on a national-level. The survey is designed to provide descriptive information on the patterns and treatment of diseases encountered in office-based physician practices in the U.S. The audit is composed of approximately 3,100 office-based physicians representing 29 specialties

across the United States that report on all patient activity during one typical workday per month. These data may include profiles and trends of diagnoses, patients, drug products mentioned during the office visit and treatment patterns. The data are then projected nationally by physician specialty and region to reflect national prescribing patterns.

The term drug uses refers to 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.

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