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: Mobic® (meloxicam, NDAs 20-938 and 21-530)
One Year Post-Pediatric Exclusivity Postmarketing Adverse Event Review
Drug Utilization Data
Pediatric Exclusivity Grant Date: April 15, 2005

****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.****

EXECUTIVE SUMMARY

This consult examines the drug utilization patterns for Mobic® (meloxicam) 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 on April 15, 2005. Outpatient drug utilization patterns were examined for the 3-year period from May 1, 2003 through April 30, 2006.

The majority of sales for Mobic® (meloxicam) was to retail settings (88.1%). Thus, we focused on outpatient drug utilization. IMS Health, National Sales Perspective™ was used to estimate the sales volume and the channels through which the sales were made. Outpatient use was measured by

audits from Verispan, LLC, Vector One®: National (VONA), Total Patient Tracker (TPT), and Physician Drug and Diagnosis Audit (PDDA).

For comparison, we evaluated prescription volume for 8 other nonsteroidal anti-inflammatory drugs: celecoxib, ibuprofen, indomethacin, naproxen, oxaprozin, rofecoxib, tolmetin, and valdecoxib. Among these selected products, Mobic® (meloxicam) ranked 4th in terms of numbers of retail prescriptions dispensed, accounting for approximately 7.4 million (11%) of the dispensed prescriptions for this group in the post-exclusivity period.

Physicians categorized as General Practice/Family Medicine/Osteopathic Medicine were the most frequent prescribers of Mobic® (meloxicam), with respect to the total number of retail prescriptions dispensed to patients of all ages. This group prescribed 29% (2.2 million) of the dispensed prescriptions during the post-exclusivity period.

In analyzing drug use patterns by total numbers of retail prescriptions dispensed, most of the prescriptions for Mobic® (meloxicam) were dispensed to adults. During the post-exclusivity period, approximately 21,000 prescriptions (0.3% of total) were dispensed to pediatric patients.

When drug use patterns were analyzed by total numbers of patients receiving prescriptions for Mobic® (meloxicam), again the majority of patients receiving prescriptions were adults. During the post-exclusivity period, pediatric patients made up 0.5% of the total number of patients. The projected number of pediatric patients receiving these prescriptions for that period was approximately 13,168. This represented a decrease of 17% from the pre-exclusivity period.

The 4 digit ICD-9 code most frequently associated with pediatric office visits in the post-exclusivity period was for ankle sprains (ICD-9 845.0), accounting for 18,000 of 32,000 visits. The 2nd most frequent code was for juvenile osteochondrosis of the leg (ICD-9 734.2), with 8,000 visits.

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. A review of drug utilization patterns for Mobic® (meloxicam) was previously conducted by the Divisional of Surveillance, Research, and Communication Support at the time of the Proposed Pediatric Study Request submitted by Boehringer Ingelheim.[*]

Mobic® (meloxicam; NDAs 20-938 & 21-530) is a nonsteroidal anti-inflammatory drug. Mobic® (meloxicam) was first approved in tablet form in the U.S. on April 13, 2000 for the relief of signs and symptoms of osteoarthritis in adults 18 years and older. It is available as 7.5mg and 15mg oral

[*] Division of Surveillance, Research, and Communication Support Project ID: D040716. Review data: November 16, 2004. Reviewers: Laura Governale, PharmD, MBA and Sigal Kaplan, PhD, BPharm.

tablets. The 7.5mg/5mL oral suspension was approved on June 1, 2004.

The FDA Pediatric Exclusivity Board granted pediatric exclusivity for Mobic® (meloxicam) on April 15, 2005. Based upon the studies completed for pediatric exclusivity, a new indication, Juvenile Rheumatoid Arthritis (JRA) in children 2 years and older, was approved on August 11, 2005. Table 1 provides a summary of the approved indications and recommended doses.

Table 1: Mobic® (meloxicam) Approved Indications and Recommended Doses[1]

Indication	Date of Approval	FDA Approved Usual Dose
Osteoarthritis, relief of signs and symptoms (adults)	April 13, 2000	7.5mg to 15mg once daily (adults)
Rheumatoid arthritis, relief of signs and symptoms (adults)	July 16, 2004	7.5mg to 15mg once daily (adults)
Juvenile Rheumatoid Arthritis, pauciarticular or polyarticular (children 2 years of age and older)	August 11, 2005	0.125mg/kg once daily to Maximum 7.5mg once daily (children aged 2 years and older)

The prevalence of JRA has been estimated at 1 per 1,000 children and the annual incidence is approximately 1 per 10,000 children[2]. Methotrexate is generally considered the primary treatment for most patients with polyarthritis[3]. NSAIDs do not modify the course of JRA; rather, they are used to treat the symptoms of JRA such as pain, stiffness, and fever.

Pediatric-specific information for JRA was added to the Mobic® label under "Clinical Pharmacology", "Clinical Trials", "Precautions" and "Adverse Reactions". The information included under Clinical Pharmacology", "Clinical Trials", and "Precautions" appears below.

CLINICAL PHARMACOLOGY
Special Populations
Pediatric
After single (0.25 mg/kg) dose administration and after achieving steady-state (0.375 mg/kg/day), there was a general trend of approximately 30% lower exposure in younger patients (2-6 years old) as compared to the older patients (7-16 years old). The older patients had meloxicam exposures similar (single dose) or slightly reduced (steadystate) to those in the adult patients, when using AUC values normalized to a dose of 0.25 mg/kg (see **DOSAGE AND ADMINISTRATION**). The meloxicam mean (SD) elimination half-life was 15.2 (10.1) and 13.0 hours (3.0) for the 2-6 year old patients, and 7-16 year old patients, respectively.

In a covariate analysis, utilizing population pharmacokinetics body-weight, but not age, was the single predictive covariate for differences in the meloxicam apparent oral plasma clearance. The body-weight normalized apparent oral clearance values were adequate predictors of meloxicam exposure in pediatric patients.

The pharmacokinetics of MOBIC in pediatric patients under 2 years of age have not been investigated.

CLINICAL TRIALS
Pauciarticular and Polyarticular Course Juvenile Rheumatoid Arthritis (JRA)
The use of MOBIC for the treatment of the signs and symptoms of pauciarticular or polyarticular course Juvenile Rheumatoid Arthritis in patients 2 years of age and older was evaluated in two 12-week, double-blind, parallel-arm, active-controlled trials. Both studies included three arms: naproxen and two doses of meloxicam. In both studies, meloxicam dosing began at 0.125 mg/kg/day (7.5 mg maximum) or 0.25 mg/kg/day (15 mg maximum), and naproxen dosing began at 10 mg/kg/day. One study used these doses throughout the 12-week dosing period, while the other incorporated a titration after 4

weeks to doses of 0.25 mg/kg/day and 0.375 mg/kg/day (22.5 mg maximum) of meloxicam and 15 mg/kg/day of naproxen.

The efficacy analysis used the ACR Pediatric 30 responder definition, a composite of parent and investigator assessments, counts of active joints and joints with limited range of motion, and erythrocyte sedimentation rate. The proportion of responders were similar in all three groups in both studies, and no difference was observed between the meloxicam dose groups.

PRECAUTIONS
Pediatric Use
The safety and effectiveness of meloxicam in pediatric JRA patients from 2 to 17 years of age has been evaluated in three clinical trials (see **CLINICAL TRIALS, ADVERSE REACTIONS** and **DOSAGE AND ADMINISTRATION** sections).

This review describes sales and outpatient drug use patterns for Mobic® (meloxicam) in adults (ages 17 years and older) and children (ages 0-16 years). The period of observation was three (3) years, from the year prior to and including the year after the granting of pediatric exclusivity (i.e., May 1, 2003 through April 30, 2006). Proprietary drug use databases licensed by the FDA 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 Mobic® (meloxicam) is sold. Sales of this product by number of extended units (i.e., combined total number of tablets and quantity of milliliters of suspension) sold to retail and non-retail channels of distribution were analyzed for three 12-month periods from May 1, 2003 through April 30, 2006 (Table 2).

Mobic® (meloxicam) appears to be sold primarily to retail settings and as the tablet form. Based on the total number of extended units of Mobic® (meloxicam) sold for the 3-year period of this analysis, most (88.1%) went to retail settings. Sales to mail order pharmacies accounted for 20.8% of all sales during the 3-year time period examined[†].

Tablets accounted for 99.9% of product sold during this 3-year period. Although the absolute quantity of suspension sold was small, for the period of this analysis in which suspension was marketed (May 1, 2005 to April 30, 2006), a larger proportion of oral suspension was sold to long term care facilities (4.5% of all oral suspension), as compared with the proportion of tablets that were sold to long term care (2.4% of all tablets)[‡].

[†] Note that the Verispan databases later used to estimate numbers of prescriptions dispensed and numbers of patients receiving those prescriptions do not currently include mail order prescriptions. Therefore those quantities may be somewhat underestimated as a national estimate of all retail prescriptions and patient counts.
[‡] IMS Health, IMS National Sales Perspectives™ Combined, MAT May 2003-April 2006. Data extracted June 2006. Original files: 0606mel4.dvr, 0606mel4.xls.

Table 2. Total Quantity of Mobic® (meloxicam) Extended Units[a] (in thousands) Sold to U.S. Distribution Channels During May 2003 through April 2006[§]

	May 2003 through April 2004		May 2004 through April 2005		May 2005 through April 2006	
	N (000)	***%***	**N (000)**	***%***	**N (000)**	***%***
Total	**149,927**	***100.0***	**285,136**	***100.0***	**374,998**	***100.0***
Retail[b]	134,432	*89.7*	250,616	*87.9*	328,899	*87.7*
Non-Retail[c]	15,495	*10.3*	34,520	*12.1*	46,100	*12.3*

[a] Extended Units are the number of individual tablets, capsules, etc. for solid dosage forms and number of grams or milliliters for other forms.
[b] Retail: chain, independent, mail order, and food store pharmacies.
[c] Non-Retail: non-federal hospitals, federal facilities, clinics, HMOs, long term care, home health care, prisons, universities, and other.

Because the bulk of drug product sales of Mobic® (meloxicam) for this time period was to retail settings, we examined additional utilization patterns for Mobic® (meloxicam) by focusing on the outpatient setting only. Outpatient drug use data were obtained from databases licensed from Verispan, LLC, Vector One®: National (VONA), Total Patient Tracker (TPT), and Physician Drug and Diagnosis Audit (PDDA) (see Appendix). These databases were used to obtain estimates of the number of drug uses by office-based physicians, the number of dispensed prescriptions by retail pharmacies and the number of patients who received a dispensed Mobic® (meloxicam) retail prescription.

Outpatient drug utilization patterns were examined for the 3-year period from May 1, 2003 through April 30, 2006. For the purpose of providing a broad perspective on Mobic® (meloxicam), we compared its utilization to that of 8 other nonsteroidal anti-inflammatory drug molecules (NSAIDs) which included celecoxib, ibuprofen, indomethacin, naproxen, oxaprozin, tolmetin, rofecoxib, and valdecoxib[**].

RESULTS

I. Dispensed Prescriptions

All Selected NSAID Products

Table 2 and Figure 1 (see Attachment 1) illustrate overall trending in total numbers of prescriptions for the 9 selected NSAID molecules that were dispensed by retail pharmacies during the period of observation.

There was a decrease in the total volume of prescriptions dispensed for this group of 9 nonsteroidal anti-inflammatory molecules during the 3-year period of observation. During the pre-exclusivity period (May 1, 2004 to April 30, 2005), 84.7 million prescriptions were dispensed by retail pharmacies in the U.S. for these 9 products (see Table 2). During the post-exclusivity period (May 1, 2005 to April 30, 2006), 66.9 million prescriptions were dispensed. This represented a 21% decrease from the pre-exclusivity period to the post-exclusivity period for the group.

On an individual drug level, two products, Vioxx® (valdecoxib) and Bextra® (rofecoxib), were withdrawn from marketing in the U.S. on September 30, 2004 and April 7, 2005, respectively. Prior

[§] IMS Health, IMS National Sales Perspectives™ Combined, MAT May 2003-April 2006. Data extracted June 2006. Original files: 0606mel2.dvr, 0606mel2.xls.
[**] Note that 2 of these products (ibuprofen and naproxen) are over-the-counter (OTC) products in the U.S. Thus the dispensed prescription volume of these OTC products will grossly underestimate their actual use.

to these withdrawals, significant and controversial safety issues associated with these and possibly other NSAID products were widely discussed and publicized. FDA Advisory Committee Meetings were held, an FDA Public Health Advisory was issued, and stronger labeling was adopted for both OTC and prescription products[4]. These events undoubtedly affected the total volume of retail prescriptions dispensed for this group of drugs.

Table 2: Total Number of Prescriptions Dispensed (in thousands) by Retail Pharmacies for Mobic® (meloxicam) and Other Selected NSAIDs[††]

	May 2003 – April 2004		May 2004 – April 2005		May 2005 – April 2006	
	TRxs (000)	Share %	TRxs (000)	Share %	TRxs (000)	Share %
TOTAL MARKET	**93,885**	**100.00%**	**84,662**	**100.00%**	**66,924**	**100.00%**
Ibuprofen (single ingredient)	**23,429**	**24.95%**	**24,538**	**28.98%**	**25,436**	**38.01%**
0-16	2,423	10.34%	2,316	9.44%	2,617	10.29%
17+	20,846	88.98%	21,947	89.44%	22,587	88.80%
UNSPEC.	160	0.68%	275	1.12%	232	0.91%
Naproxen, naproxen sodium (including lansoprazole)	**15,710**	**16.73%**	**15,689**	**18.53%**	**15,626**	**23.35%**
0-16	582	3.71%	541	3.45%	489	3.13%
17+	15,033	95.69%	15,012	95.69%	15,019	96.12%
UNSPEC.	94	0.60%	136	0.86%	117	0.75%
Celebrex® (celecoxib)	**18,678**	**19.90%**	**16,498**	**19.49%**	**10,960**	**16.38%**
0-16	52	0.28%	42	0.25%	25	0.23%
17+	18,519	99.14%	16,316	98.89%	10,858	99.07%
UNSPEC.	108	0.58%	141	0.85%	77	0.70%
Mobic® (meloxicam)	**2,972**	**3.17%**	**5,673**	**6.70%**	**7,375**	**11.02%**
0-16	14	0.48%	22	0.39%	21	0.29%
17+	2,939	98.87%	5,618	99.02%	7,325	99.32%
UNSPEC.	19	0.65%	33	0.59%	29	0.39%
Indomethacin	**3,186**	**3.39%**	**3,339**	**3.94%**	**3,530**	**5.27%**
0-16	20	0.64%	20	0.60%	20	0.57%
17+	3,142	98.62%	3,292	98.59%	3,488	98.82%
UNSPEC.	23	0.74%	27	0.81%	22	0.61%
Ibuprofen (w/narc analgesics)	**2,511**	**2.67%**	**2,442**	**2.88%**	**2,715**	**4.06%**
0-16	27	1.09%	25	1.02%	27	0.98%
17+	2,468	98.30%	2,399	98.26%	2,674	98.49%
UNSPEC.	15	0.61%	18	0.72%	14	0.53%
Oxaprozin	**872**	**0.93%**	**1,028**	**1.21%**	**1,206**	**1.80%**
0-16	6	0.67%	7	0.68%	7	0.56%
17+	861	98.81%	1,012	98.45%	1,190	98.72%
UNSPEC.	5	0.52%	9	0.87%	9	0.73%
Tolmetin sodium	**89**	**0.09%**	**81**	**0.10%**	**75**	**0.11%**
0-16	4	4.88%	3	4.21%	3	3.80%
17+	84	94.59%	77	95.13%	71	95.51%
UNSPEC.	0	0.53%	1	0.67%	1	0.68%
Bextra® (valdecoxib)	**9,690**	**10.32%**	**8,961**	**10.58%**	**1**	**0.00%**
0-16	44	0.45%	35	0.39%	0	0.46%
17+	9,577	98.83%	8,866	98.94%	1	94.38%
UNSPEC.	69	0.72%	61	0.68%	0	5.16%
Vioxx® (rofecoxib)	**16,748**	**17.84%**	**6,415**	**7.58%**	**0**	**0.00%**
0-16	91	0.55%	34	0.52%	--	--
17+	16,580	98.99%	6,339	98.83%	0	69.32%
UNSPEC.	77	0.46%	42	0.65%	0	30.68%

[††] Verispan, LLC, VONA®. May 2003 – April 2006. Data extracted June 2006. Files: VONA0606NSAIDs_Age.qry

Pediatric use (i.e., patients aged 0 to 16 years) for most of these products was significantly lower than the proportion of prescriptions that were dispensed for adults 17 years and older. For the post-exclusivity period (May 2005 to April 2006), ibuprofen (single ingredient) and naproxen had the largest volume of pediatric use, even with the known underestimation of OTC drug use. All other NSAID molecules, (with the exception of tolmetin sodium, with 3.8%), had pediatric prescription volumes of less than 1% for that period.

Mobic® (meloxicam)

During the post-exclusivity period (May 2005 to April 2006), Mobic® (meloxicam) ranked 4th in terms of the numbers of prescriptions dispensed for this group of 9 drug substances, accounting for approximately 11% of the dispensed prescriptions for the selected NSAID products analyzed.

The total number of dispensed retail prescriptions for Mobic® (meloxicam) increased from approximately 5.7 million prescriptions in the pre-exclusivity period (May 2004 to April 2005) to approximately 7.4 million prescriptions in the post-exclusivity period (May 2005 to April 2006). This represented a 30% increase from the pre-exclusivity period to the post-exclusivity period.

II. Prescriber Specialty

The group of physicians categorized as General Practice/Family Medicine/Osteopathic Medicine were the most frequent prescribers of Mobic® (meloxicam) in all three periods of observation (Table 3). In the post-exclusivity period (May 2005 to April 2006), this group prescribed approximately 2.2 million (29.4%) of the meloxicam prescriptions dispensed in the retail pharmacy setting. Internal Medicine physicians were the 2nd most frequent prescribers, with approximately 1.9 million dispensed prescriptions (25.1%) for the same period. Rheumatologists ranked 4th and prescribed approximately 578,000 dispensed prescriptions in the same period (7.8%). For this post-exclusivity period, the top 5 specialty groups accounted for 81% of the dispensed prescriptions for Mobic® (meloxicam) in the post-exclusivity period.

Pediatricians ranked 14th in terms of prescription volume and prescribed 54,000 (0.7%) of the Mobic® (meloxicam) retail prescriptions dispensed during the post-exclusivity period.

Table 3: Total Number of Retail Prescriptions Dispensed (in thousands) for Mobic® (meloxicam) by Prescriber Specialty[‡‡].

Prescriber Specialty	May 2003 – April 2004		May 2004 – April 2005		May 2005 – April 2006	
	TRxs (000)	%	TRxs (000)	%	TRxs (000)	%
ALL PRESCRIBERS	2,972	*100%*	5,673	*100%*	7,375	*100%*
1. General Practice/ Family Medicine/ Osteopathic Med	885	*29.8%*	1,658	*29.2%*	2,170	*29.4%*
2. Internal Medicine	701	*23.6%*	1,370	*24.2%*	1,854	*25.1%*
3. Orthopedic Surgery	398	*13.4%*	714	*12.6%*	895	*12.1%*
4. Rheumatology	309	*10.4%*	500	*8.8%*	578	*7.8%*
5. Specialty Unspecified	220	*7.4%*	455	*8.0%*	496	*6.7%*
14. Pediatrics	19	*0.6%*	40	*0.7%*	54	*0.7%*
All Others	441	*14.8%*	937	*16.5%*	1,330	*18.0%*

‡‡ Source: Verispan, LLC, VONA. May 2003 to April 2006. Data extracted June 2006. File: VONA0606melox_MDs.qry.

III. Patient Demographics

The total number of retail prescriptions for Mobic® (meloxicam) dispensed to the pediatric population (ages 0 – 16 years) was approximately 22,000 prescriptions for the pre-exclusivity period (Table 4). There was no significant change in the post-exclusivity period, when approximately 21,000 prescriptions were dispensed. Mobic® (meloxicam) prescriptions dispensed to the pediatric population aged 0-16 years old accounted for 0.3% of the total dispensed Mobic® prescriptions during the post-exclusivity period.

Mobic® oral tablet dosage forms accounted for the majority of the dispensed pediatric prescriptions.

Table 4. Total Number of Retail Prescriptions Dispensed (in thousands) for Mobic® (meloxicam) by Age Group[§§]

	May 2003 – April 2004		May 2004 – April 2005		May 2005 – April 2006	
	TRxs (000)	%	TRxs (000)	%	TRxs (000)	%
TOTAL	2,972	*100%*	5,673	*100%*	7,375	*100%*
0 to 16 years old	14	*0.5%*	22	*0.4%*	21	*0.3%*
Tablets	14	*100%*	22	*100%*	21	*98.4%*
Suspension	--	--	--	--	<1	*1.6%*
17 years and older	2,939	*98.9%*	5,618	*99.0%*	7,325	*99.3%*
Age Unspecified	19	*0.6%*	33	*0.6%*	29	*0.4%*

The projected number of patients of all ages per year who received a dispensed retail prescription for Mobic® (meloxicam) increased from approximately 2.6 million patients in the pre-exclusivity period to 2.7 million patients in the post-exclusivity period (Table 5). This represented an increase of approximately 4%.

Table 5. Total Number of Patients Receiving Prescriptions for Mobic® (meloxicam) Dispensed by Retail Pharmacies by Age Group[***]

Age Groups	May 2003 - April 2004		May 2004 - April 2005		May 2005 - April 2006	
	Projected Patient Count	Total Patient Share	Projected Patient Count	Total Patient Share	Projected Patient Count	Total Patient Share
Grand Total	1,214,567	*100%*	2,559,424	*100%*	2,668,264	*100%*
0 to 16 years	9,846	*0.81%*	15,786	*0.62%*	13,168	*0.49%*
17 and older	1,194,647	*98.36%*	2,522,073	*98.54%*	2,638,233	*98.87%*
Unknown age	19,229	*1.58%*	39,906	*1.44%*	36,407	*1.36%*

The projected number of pediatric patients aged 0 to 16 years who received a dispensed prescription for Mobic® (meloxicam) decreased slightly from the pre-exclusivity period to the post-exclusivity period, from 15,786 to 13,168 patients.

[§§] Source: Verispan, LLC: VONA. May 2003 to April 2006. Data extracted June 2006. File: VONA0606melox_Age_Form.qry.
[***] Verispan, LLC: Total Patient Tracker (TPT). Data extracted June 2006. File: TPT0606Mobic_age.xls.

IV. Indication for Use

Less than 1% of the drug uses during the post-exclusivity period for Mobic® (meloxicam) (May 2005 to April 2006) were for pediatric patients.

The 4 digit ICD-9 code most frequently associated with Mobic® (meloxicam) office-based physician visits in the pediatric population (0-16 years) during this three-year period was ankle sprains (ICD-9 code 845.0) (Table 6). For the post-exclusivity period, there were 32,000 total pediatric drug uses. Ankle sprains made up approximately 18,000 (55%) of these drug uses. The 2nd most frequent code was for juvenile osteochondrosis of the leg (ICD-9 734.2), with 8,000 uses (25%) during this time period.

The 4 digit ICD-9 code most frequently associated with Mobic® (meloxicam) office-based physician visits in adults aged 17 and older was osteoarthrosis, NOS (ICD-9 code 715.9). For the post-exclusivity period, there were 5.9 million adult drug uses. Osteoarthrosis, NOS made up approximately 1.2 million (21%) of these drug uses.

Table 6: Five Most Frequent ICD-9 Codes Associated with Uses of Mobic® (meloxicam) (in thousands) During Office-Based Physician Visits, by Patient Age Groups[†††]

	May 2003 – April 2004		May 2004 – April 2005		May 2005 – April 2006	
	Uses	Share	Uses	Share	Uses	Share
	(000)	%	(000)	%	(000)	%
All Mobic® (meloxicam)	2,663	*100.00%*	5,910	*100.00%*	6,127	*100.00%*
0-16 years of age	32	*1.19%*	56	*0.95%*	32	*0.53%*
8450 SPRAIN OF ANKLE	--	--	12	*22.13%*	18	*54.98%*
7324 JUV OSTEOCHONDROSIS LEG	--	--	7	*11.55%*	8	*25.08%*
8449 SPRAIN OF KNEE & LEG NOS	--	--	--	--	6	*19.94%*
9593 ELB/FOREARM/WRST INJ NOS	6	*17.83%*	--	--	--	--
8442 SPRAIN CRUCIATE LIG KNEE	8	*24.07%*	--	--	--	--
All Others	18	*58.10%*	37	*66.31%*	--	--
17 years and older	2,497	*93.76%*	5,662	*95.81%*	5,926	*96.71%*
7159 OSTEOARTHROSIS NOS	553	*22.15%*	1,001	*17.68%*	1,220	*20.59%*
7242 LUMBAGO	134	*5.37%*	224	*3.95%*	357	*6.02%*
7169 ARTHROPATHY NOS	65	*2.59%*	337	*5.95%*	346	*5.84%*
7194 PAIN IN JOINT	127	*5.08%*	337	*5.95%*	311	*5.25%*
7287 OTHER FIBROMATOSES	139	*5.57%*	225	*3.97%*	228	*3.85%*
All Others	1,479	*59.24%*	3,539	*62.49%*	3,464	*58.45%*
Age Unspecified	135	*5.06%*	191	*3.24%*	169	*2.76%*
7159 OSTEOARTHROSIS NOS	7	*5.27%*	24	*12.41%*	21	*12.50%*
7261 ROTATOR CUFF SYNDR ET AL	4	*3.20%*	7	*3.75%*	17	*9.87%*
7291 MYALGIA AND MYOSITIS NOS	8	*5.77%*	--	--	14	*8.40%*
7269 ENTHESOPATHY NOS	--	--	--	--	14	*8.38%*
8404 SPRAIN ROTATOR CUFF	--	--	--	--	11	*6.57%*
All Others	115	*85.75%*	161	*83.84%*	92	*54.28%*

[†††] Verispan, LLC: Physician Drug & Diagnosis Audit (PDDA). Data extracted June 2006. File: PDDA0606melox_dx4_age.qry

DISCUSSION

The majority of sales for Mobic® (meloxicam) was to retail settings (88.1%). Thus, we focused on outpatient drug utilization. We also evaluated prescription volume for 8 other nonsteroidal anti-inflammatory drugs: celecoxib, ibuprofen, indomethacin, naproxen, oxaprozin, rofecoxib, tolmetin, and valdecoxib.

Among these selected products, Mobic® (meloxicam) ranked 4th in terms of numbers of retail prescriptions dispensed, accounting for approximately 7.4 million (11%) of the dispensed prescriptions for this group in the post-exclusivity period.

Physicians categorized as General Practice/Family Medicine/Osteopathic Medicine were the most frequent prescribers of Mobic® (meloxicam), with respect to the total number of retail prescriptions dispensed to patients of all ages.

In analyzing drug use patterns by total numbers of retail prescriptions dispensed, most of the prescriptions for Mobic® (meloxicam) were dispensed to adults. During the post-exclusivity period, 0.3% of all retail prescriptions were dispensed to pediatric patients.

When drug use patterns were analyzed by total numbers of patients receiving prescriptions for Mobic® (meloxicam), again the majority of patients receiving prescriptions were adults. During the post-exclusivity period, pediatric patients made up 0.5% of the total number of patients.

The 4 digit ICD-9 code most frequently associated with pediatric office visits in the post-exclusivity period was for ankle sprains (ICD-9 845.0), with 18,000 of 32,000 visits. The 2nd most frequent code was for juvenile osteochondrosis of the leg (ICD-9 734.2), with 8,000 visits.

Limitations

Findings from this consult should be interpreted in the context of the known limitations of the databases used. We estimated that the use of meloxicam was primarily in the outpatient settings based on the IMS Health, National Sales Perspectives™. 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 the facilities purchase drugs in quantities reflective of actual patient use.

PDDA 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, as in the case of meloxicam.

While we conducted a comprehensive analysis of the use of this product in the outpatient settings, in which the majority of use occurred, use outside of the retail pharmacy settings was not captured in our analysis.

CONCLUSION

Although the clinical trial data submitted for approval of Pediatric Exclusivity for Mobic® (meloxicam) resulted in a labeling change which allowed for marketing of a new indication, Juvenile rheumatoid arthritis (JRA), a very small proportion and volume of the total number of patients and total numbers of prescriptions for this drug are pediatric.

The prevalence of JRA has been estimated at 1 per 1,000 children and the annual incidence is approximately 1 per 10,000 children[2]. Currently, methotrexate is generally considered the primary treatment for most patients with polyarthritis[3]. NSAIDs do not modify the course of JRA; rather, they are used to treat the pain and stiffness due to JRA[3]. This new indication was approved 4 months after the granting of pediatric exclusivity. Thus, the product has been approved for marketing in the pediatric population for only 8 months of the post-exclusivity period. Several NSAIDs are available in the U.S., and recently a great deal of controversy and media attention has surrounded the safety of the NSAIDs in general. These factors may have affected the volume and proportion of Mobic® (meloxicam) that is prescribed for children with JRA in the U.S.

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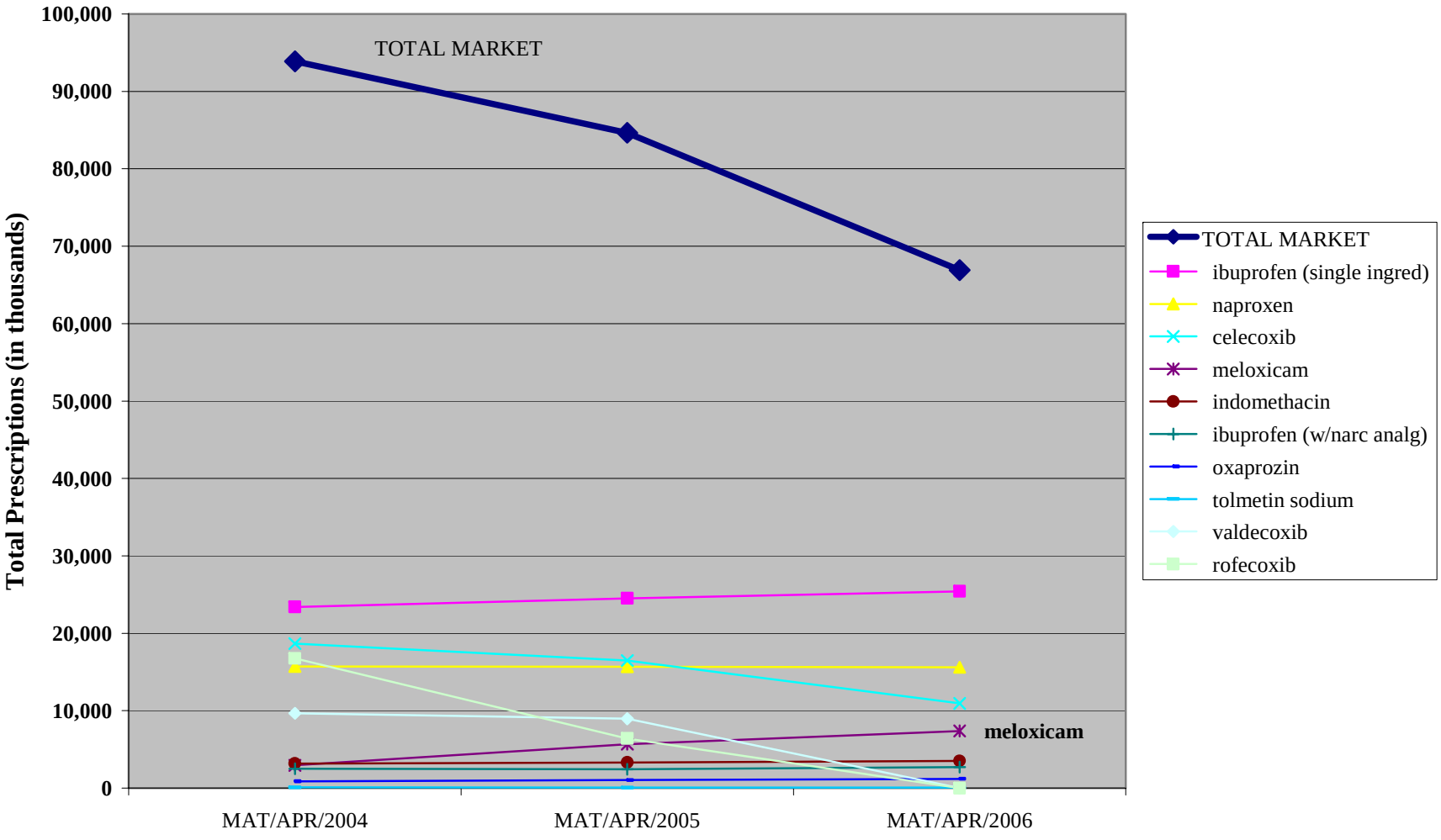
Attachment 1

Total Prescriptions Dispensed (in Thousands) by Retail Pharmacies:
Moving Annual Totals May 2003 - April 2006



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. 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.

Data for this analysis include prescriptions dispensed for Mobic® (meloxicam) and the other NSAIDs from May 1, 2004 to April 30, 2006, inclusive.

VERISPAN, LLC

Vector One®: 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® 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 2.0 billion prescription claims, 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.

Data for this analysis include prescriptions dispensed for Mobic® (meloxicam) and the other NSAIDs from May 1, 2004 to April 30, 2006, 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 2.0 billion prescription claims per year, which represents over 160 million patients tracked across time.

Data for this analysis include prescriptions dispensed for Mobic® (meloxicam) and the other NSAIDs from May 1, 2004 to April 30, 2006, inclusive.

VERISPAN, LLC
Vector One®: Physician Drug and 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.

Verispan uses the term "drug uses" to refer 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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[1] Mobic® (meloxicam, Boehringer Ingelheim) Complete Prescribing Information. Revised August 10, 2005.
[2] Mason TG and Reed AM. Update in juvenile rheumatoid arthritis. Arthritis Rheum 2005; 53(5):796-9.
[3] Hashkes PJ and Laxer RM. Medical treatment of juvenile rheumatoid arthritis. 2005;294(13):1671-84.
[4] US Food and Drug Administration. http://www.fda.gov/cder/drug/infopage/COX2/default.htm

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/s/

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