

**MEMORANDUM**

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

**PID#:** 2007-43

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**SUBJECT:** Lescol and Lescol XL<sup>®</sup> (fluvastatin); NDA 20-261/S-036, 21-192/S-011  
One Year Post-Pediatric Exclusivity Postmarketing Adverse Event Review:  
Drug Utilization Data  
Pediatric Exclusivity Grant Date: December 15, 2005

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**\*\*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

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This consult examines the drug utilization patterns for Lescol and Lescol XL<sup>®</sup> (fluvastatin) in the pediatric groups aged 9-16 years, with primary focus on patterns of use two years before and one year following the granting of Pediatric Exclusivity on December 15, 2005. Lescol and Lescol XL<sup>®</sup> (fluvastatin) is an oral HMG-CoA reductase inhibitor used to reduce elevated total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), and apolipoprotein B (apo-B) levels and to increase high density lipoprotein cholesterol (HDL-C) levels.

Proprietary drug use databases licensed by FDA were used to conduct this analysis. The IMS Health, IMS National Sales Perspectives<sup>™</sup> was used to determine the various retail and non-retail channels of distribution. Indications for outpatient use were measured by Verispan's Physician Drug and Diagnosis Audit (PDDA), while retail prescriptions, patient counts and demographics were measured by Verispan's Vector One<sup>®</sup>: National (VONA) and Total Patient Tracker (TPT). We examined outpatient drug use patterns for Lescol and Lescol XL<sup>®</sup> (fluvastatin) for the three 1-year periods from January 1, 2004 through December 30, 2006.

The examination of wholesale sales data indicates that approximately 94% of fluvastatin was distributed to outpatient retail pharmacy settings. Retail pharmacies (chain, independent, and food stores with pharmacies) accounted for over 66% of overall sales while mail order pharmacies accounted for approximately 27% of sales during year 2005.

There was an approximate 8% increase in the number of total dispensed prescriptions for HMG-CoA reductase inhibitors class (atorvastatin, lovastatin, pravastatin, simvastatin, rosuvastatin, and fluvastatin) from approximately 118 million prescriptions during the pre-exclusivity period of January 2005 – December 2005 to close to 128 million prescriptions during the post-exclusivity period (January 2006 to December 2006). There was no significant change in the number of total dispensed prescriptions for many of the other classes within the cholesterol market from the pre-exclusivity period of January 2005 – December 2005 to the post-exclusivity period. However, there was an 81% increase in the number of total dispensed prescriptions for the Cholesterol Reducers Combination Class.

Fluvastatin was the least commonly dispensed product of the six currently marketed statins and accounted for approximately 2% to 4% of the HMG-CoA reductase inhibitor market in each of the three 1-year time periods. There was an approximate 24% decrease in the number of total dispensed prescriptions for fluvastatin from the pre-exclusivity period of January 2005 – December 2005 to the post-exclusivity period. The overall number of prescriptions dispensed for fluvastatin decreased from approximately 4.7 million prescriptions during the pre-exclusivity period of January 2004 – December 2004 to 3.9 million prescriptions during the pre-exclusivity period of January 2005 – December 2005 and again to approximately 3 million prescriptions during the post-exclusivity period. The share of dispensed fluvastatin prescriptions to the pediatric age group represented approximately 0.02% of the total dispensed prescriptions for fluvastatin during all three 1-year time periods. There was no significant change in number of fluvastatin prescriptions dispensed to the pediatric population during this time period.

General Practitioners and Internal Medicine specialties were the most frequent prescribers of fluvastatin and together accounted for approximately 77% of all dispensed prescriptions during the entire study period. The indication for use most frequently linked to fluvastatin in adults was "Disorder of Lipoid Metabolism" (ICD-9 272.0). No indications for use were linked to patients aged 0-16 years during the study period.

## INTRODUCTION

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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 review 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 soon after the one-year anniversary of granting exclusivity. This review is in addition to the routine post-marketing safety surveillance activities the FDA performs for all marketed drugs.

Fluvastatin (Lescol<sup>®</sup> NDA 20-261 and Lescol XL<sup>®</sup> NDA 21-192) is an oral HMG-CoA reductase inhibitor. Lescol<sup>®</sup> and Lescol XL<sup>®</sup> are indicated to reduce elevated total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), and apolipoprotein B (apo-B) levels and to increase high density lipoprotein cholesterol (HDL-C) levels in patients with primary hypercholesterolemia (heterozygous familial and non familial) and mixed dyslipidemia Fredrickson Type IIa and IIb) whose response to dietary restriction of saturated fat and cholesterol and other nonpharmacological measures has not been adequate. Lescol<sup>®</sup> and Lescol XL<sup>®</sup> are indicated to reduce the risk of undergoing coronary revascularization procedures (secondary prevention of coronary events). Lescol<sup>®</sup> and Lescol XL<sup>®</sup> are indicated as an adjunct to diet to slow the progression of coronary atherosclerosis in patients with coronary heart disease as a part of treatment strategy to lower total and LDL cholesterol to target levels. On April 10, 2006, Lescol<sup>®</sup> and Lescol XL<sup>®</sup> were approved for reduction of total-C, LDL-C, and apo-B levels in adolescent girls who are at least one year post-menarche and boys, 10-16 years of age, with heterozygous familial hypercholesterolemia whose response to dietary restriction has not been adequate, under NDA 20-261/S-036 and NDA 21-192/S-011.

The Pediatric Exclusivity Board of the FDA granted pediatric exclusivity for Lescol<sup>®</sup> and Lescol XL<sup>®</sup> (fluvastatin; NDA 20-261 and NDA 21-192) on December 15, 2005. On April 10, 2006, Lescol<sup>®</sup> and Lescol XL<sup>®</sup> were approved under NDA 20-261/S-036 and NDA 21-192/S-011 for use in the pediatric population based on two open-label, uncontrolled, dose-titration studies which enrolled pediatric patients with heterozygous familial hypercholesterolemia. The first study enrolled 29 pre-pubertal boys, 9-12 years of age. The second study enrolled 85 male and female patients, 10 to 16 years of age.<sup>1</sup>

This review describes outpatient drug use patterns for Lescol<sup>®</sup> and Lescol XL<sup>®</sup> (fluvastatin) for the three 1-year periods from January 1, 2004 through December 30, 2006. Proprietary drug use databases licensed by the FDA were used to conduct this analysis.

## METHODS

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IMS Health, IMS National Sales Perspectives<sup>™</sup> data (see Appendix) were used to determine the setting in which fluvastatin (Lescol<sup>®</sup> and Lescol XL<sup>®</sup>) is sold. Sales of this product by number of tablets or capsules sold from the manufacturer into the various retail and non-retail channels of distribution were analyzed for three years from January 2004 through November 2006. From these data, it was clear that this product is distributed to outpatient settings of care (chain, independent, food store, and mail order pharmacies) which accounted for approximately 94% of the total number of tablets/capsules sold in each of the three 1-year periods in this analysis<sup>2</sup>. Retail pharmacies (chain, independent, and food stores with pharmacies) accounted for approximately 66% of overall sales where as mail order pharmacies accounted for approximately 27% of sales during year 2005 (data not shown).

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<sup>1</sup> Lescol<sup>®</sup> and Lescol XL<sup>®</sup> were approved under NDA 20-261/S-036 and NDA 21-192/S-011 approval letter and product labeling dated April 10, 2006.

<sup>2</sup> IMS Health, IMS National Sales Perspectives<sup>™</sup>, Data extracted 1-11-2007, File: 0701fluv.dvr

Because the bulk of drug product sales of Lescol<sup>®</sup> and Lescol XL<sup>®</sup> for this time period were to outpatient retail settings, we examined the utilization patterns for Lescol<sup>®</sup> and Lescol XL<sup>®</sup> and other HMG-CoA reductase inhibitors focusing on the outpatient setting only.

Outpatient use and patient demographics were measured with two data sources from Verispan, LLC: Vector One<sup>®</sup>: National (VONA) and Total Patient Tracker (TPT). Indications for use were obtained from the Physician's Drug and Diagnosis Audit (see Appendix). Estimates of the number of drug mentions by office-based physicians, the number of dispensed prescriptions by retail pharmacies and the number of patients<sup>3</sup> who received a dispensed Lescol<sup>®</sup> and Lescol XL<sup>®</sup> retail prescription were obtained. Outpatient drug utilization patterns were examined for the 3-year period from January 1, 2004 through December 30, 2006.

## RESULTS

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### I. Dispensed Prescriptions

HMG-CoA reductase inhibitors (atorvastatin, lovastatin, pravastatin, simvastatin, rosuvastatin, and fluvastatin) accounted for 70% of the total cholesterol market share for dispensed prescriptions in the year 2006. There was a significant increase in the volume of prescriptions dispensed for HMG-CoA reductase inhibitors over the 3 years of this analysis. During the pre-exclusivity period of January 2005 – December 2005, an approximate 118 million prescriptions were dispensed by retail pharmacies in the U.S. for these HMG-CoA reductase inhibitors. During the post-exclusivity period (January 2006 to December 2006), nearly 128 million prescriptions were dispensed for these for HMG-CoA reductase inhibitors. This represented an 8.2% increase from the pre-exclusivity period to the post-exclusivity period (**Table 1**).

Other agents within the cholesterol market commonly used in the pediatric population for hypercholesterolemia include cholestyramine, colestipol, and niacin. From the pre-exclusivity period of January 2005 – December 2005 to the post-exclusivity period, there was not a significant change in the number of total dispensed prescriptions for the Bile Acid Sequestrants class or for many of the other classes within the cholesterol market. However, there was an 81% increase in the number of total dispensed prescriptions for the Cholesterol Reducers Combination Class.

Fluvastatin was the least commonly dispensed product of the six currently marketed statins and accounted for approximately 2% to 4% of the HMG-CoA reductase inhibitor market in each of the three 1-year time periods. Atorvastatin was the most commonly dispensed HMG-CoA reductase inhibitor over the 3-year analysis period (**Table 1**).

There was a significant decrease in the volume of prescriptions dispensed for fluvastatin over the 3-year period of this analysis. The overall number of prescriptions dispensed for fluvastatin decreased from approximately 4.7 million prescriptions (95% CI 4,733,000 – 4,743,000) during the pre-exclusivity period of January 2004 – December 2004 to 3.9 million prescriptions (95% CI 3,930,000 – 3,940,000) during the pre-exclusivity period of January 2005 – December 2005 and again decreased to approximately 3 million prescriptions (95% CI 3,002,000 – 3,010,000) during the post-exclusivity period. From the pre-exclusivity period of January 2005 – December 2005 to the post-exclusivity period, there was an approximate 24% decrease in the number of total dispensed fluvastatin prescriptions (**Table 1**). The share of dispensed fluvastatin prescriptions to the pediatric age group represented approximately 0.02% of the total dispensed fluvastatin prescriptions during all three 1-year time periods. There was no significant

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<sup>3</sup> Note that data concerning the total number of patients based on Verispan's Total Patient Tracker may not be summed due to aging of patients during the study period.

change in the number of prescriptions dispensed to the pediatric population during this time period (Table 2).

	2004		2005		2006	
	TRxs	Share	TRxs	Share	TRxs	Share
<b>TOTAL CHOLESTEROL MARKET</b>	<b>147,655</b>	<b>100%</b>	<b>159,624</b>	<b>100%</b>	<b>182,229</b>	<b>100%</b>
<b>HMG-CoA Reductase Inhibitors</b>	<b>117,716</b>	<b>79.7%</b>	<b>118,007</b>	<b>73.9%</b>	<b>127,567</b>	<b>70.0%</b>
Atorvastatin calcium	62,541	53.1%	63,219	53.6%	62,311	48.8%
Simvastatin	23,804	20.2%	22,325	18.9%	27,840	21.8%
Lovastatin	8,239	7.0%	10,998	9.3%	14,463	11.3%
Rosuvastatin calcium	6,359	5.4%	7,797	6.6%	11,410	8.9%
Pravastatin sodium	12,035	10.2%	9,733	8.2%	8,536	6.7%
Fluvastatin sodium	4,738	4.0%	3,935	3.3%	3,006	2.4%
cerivastatin sodium	0	0.0%	0	0.0%	0	0.0%
<b>Cholest Redcrs Combo</b>	<b>1,794</b>	<b>1.2%</b>	<b>9,278</b>	<b>5.8%</b>	<b>16,862</b>	<b>9.3%</b>
<b>Fibric Acid Derivtv</b>	<b>13,599</b>	<b>9.2%</b>	<b>14,428</b>	<b>9.0%</b>	<b>16,042</b>	<b>8.8%</b>
<b>Cholest Absorptn Inhib</b>	<b>8,427</b>	<b>5.7%</b>	<b>10,453</b>	<b>6.5%</b>	<b>12,272</b>	<b>6.7%</b>
<b>Antihyperlidemics Other</b>	<b>3,867</b>	<b>2.6%</b>	<b>4,327</b>	<b>2.7%</b>	<b>5,335</b>	<b>2.9%</b>
<b>Bile Acid Sequestrants</b>	<b>2,055</b>	<b>1.4%</b>	<b>2,020</b>	<b>1.3%</b>	<b>2,134</b>	<b>1.2%</b>
<b>Vasc/Antihyperlip Cmbo</b>	<b>191</b>	<b>0.1%</b>	<b>1,106</b>	<b>0.7%</b>	<b>2,014</b>	<b>1.1%</b>
<b>Lipotropics</b>	<b>5</b>	<b>0.0%</b>	<b>5</b>	<b>0.0%</b>	<b>4</b>	<b>0.0%</b>

Verispan, LLC, Vector One® National (VONA) Data extracted 1-17-2007  
Source File: 2007-43 VONA 1-17-07 cholesterol market 2004-2006.qry

	2004		2005		2006	
	TRxs	Share	TRxs	Share	TRxs	Share
<b>Fluvastatin Sodium</b>	<b>4,737,947</b>	<b>100.0%</b>	<b>3,935,308</b>	<b>100.0%</b>	<b>3,005,701</b>	<b>100.0%</b>
Ages 0-8 years	1,481	0.0%	930	0.0%	390	0.0%
Ages 9-16 years	714	0.0%	404	0.0%	260	0.0%
Ages 17+ years	4,708,516	99.4%	3,910,565	99.4%	2,997,362	99.7%
Unspecified age	27,236	0.6%	23,409	0.6%	7,689	0.3%

Verispan, LLC, Vector One® National (VONA) Data extracted 2-21-2007  
Source File: 2007-43 VONA 2-21-07 fluvastatin age 2004-2006 UNROUNDED.qry

## II. Patient Demographics

During the pre-exclusivity period of January 2004 – December 2004, approximately 2,000 prescriptions were dispensed to the pediatric population (ages 0 – 16 years). This decreased to approximately 1,000 prescriptions dispensed during the pre-exclusivity period for year 2005. A negligible amount of retail prescriptions were dispensed for fluvastatin to the pediatric population during the post-exclusivity period. The share of dispensed prescriptions to the pediatric age group represented an average of 0.03% of the total dispensed prescriptions for fluvastatin during all three 1-year time periods. On average, approximately 99% of fluvastatin prescriptions were dispensed to adults aged 17 years and older and, of

note, approximately 0.6% of prescriptions dispensed were to an unspecified age band during all three 1-year time periods (**Table 2**).

The projected number of all unique patients receiving a prescription for Lescol<sup>®</sup> or Lescol XL<sup>®</sup> (fluvastatin) in the retail pharmacy setting decreased from 911,037 patients during the pre-exclusivity period of January 2004 – December 2004 to 723,956 patients during the pre-exclusivity period of January 2005 – December 2005. This represented an approximate 20% decrease in the projected number of patients receiving a prescription for Lescol<sup>®</sup> or Lescol XL<sup>®</sup> (fluvastatin) in the retail pharmacy setting. There was an approximate 24% decrease in the projected number of patients from the pre-exclusivity period of January 2005 – December 2005 to 551,790 patients in the post exclusivity period (**Table 3**).

The pediatric group aged 0-8 years experienced a 62% decline in the number of patients receiving a prescription for Lescol<sup>®</sup> or Lescol XL<sup>®</sup> (fluvastatin) from 376 patients during the pre-exclusivity period of January 2005 – December 2005 to 142 patients during the post-exclusivity period. The pediatric group aged 9-16 years experienced a 31% decline in the number of patients receiving a prescription for Lescol<sup>®</sup> or Lescol XL<sup>®</sup> (fluvastatin) from 160 patients during the pre-exclusivity period of January 2005 – December 2005 to 110 patients during the post-exclusivity period. In adults age 17 years and older, the number of patients receiving a prescription for Lescol<sup>®</sup> or Lescol XL<sup>®</sup> (fluvastatin) decreased by almost 23% from 717,295 patients during the pre-exclusivity period of January 2005 – December 2005 to approximately 549,112 patients during the post-exclusivity period. Similar to the dispensed prescription data, pediatric patients represented less than 1% of the total number of patients receiving a prescription for Lescol<sup>®</sup> or Lescol XL<sup>®</sup> in the outpatient retail pharmacy setting (**Table 3**).

Age Group	Product Brand	MAT 2004		MAT 2005		MAT 2006	
		Projected Patient Count	Total Patient Share	Projected Patient Count	Total Patient Share	Projected Patient Count	Total Patient Share
<b>GRAND TOTAL</b>		<b>911,037</b>	<b>100%</b>	<b>723,956</b>	<b>100%</b>	<b>551,790</b>	<b>100%</b>
<b>0 – 8 years</b>	<b>AGE GROUP TOTAL</b>	<b>615</b>	<b>0.07%</b>	<b>376</b>	<b>0.05%</b>	<b>142</b>	<b>0.03%</b>
	Lescol	194	31.51%	135	35.97%	66	46.16%
	Lescol XL	437	70.97%	256	68.09%	68	47.72%
<b>9 – 16 years</b>	<b>AGE GROUP TOTAL</b>	<b>233</b>	<b>0.03%</b>	<b>160</b>	<b>0.02%</b>	<b>110</b>	<b>0.02%</b>
	Lescol	111	47.55%	44	27.48%	42	37.85%
	Lescol XL	126	54.04%	121	76.06%	72	65.45%
<b>17 – 85 years</b>	<b>AGE GROUP TOTAL</b>	<b>902,386</b>	<b>99.05%</b>	<b>717,295</b>	<b>99.08%</b>	<b>549,112</b>	<b>99.51%</b>
	Lescol	336,114	37.25%	241,170	33.62%	180,060	32.79%
	Lescol XL	590,400	65.43%	491,434	68.51%	377,842	68.81%
<b>Unknown Age</b>	<b>AGE GROUP TOTAL</b>	<b>26,701</b>	<b>2.93%</b>	<b>24,293</b>	<b>3.36%</b>	<b>15,318</b>	<b>2.78%</b>
	Lescol	12,979	48.61%	10,648	43.83%	6,863	44.81%
	Lescol XL	14,042	52.59%	13,870	57.09%	8,511	55.56%

Verispan, Total Patient Tracker, data extracted 1/18/07 (MAT 2004, 2005) and 1/23/07 (MAT 2006)  
Source files: 2007-43 TPT 1-18-07 fluvastatin age MAT 2004.xls, 2007-43 TPT 1-18-07 fluvastatin age MAT 2005.xls, 2007-43 TPT 1-23-07 fluvastatin age MAT 2006.xls  
\*Subtotals may not sum exactly, due to rounding error. 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.

### III. Prescriber Specialty

General Practitioners and Internal Medicine specialties were the two most frequent prescribers of Lescol<sup>®</sup> or Lescol XL<sup>®</sup> (fluvastatin) in each of the three 1-year periods of observation, accounting for approximately 40% and 37-38% of retail prescriptions, respectively (**Table 4**). Cardiologists accounted for no more than 7% of prescribers in the entire 36-month period, while pediatricians accounted for less than 1% of prescriptions during all three time periods.

	2004		2005		2006	
	TRxs	Share	TRxs	Share	TRxs	Share
<b>Fluvastatin Sodium</b>	<b>4,738</b>	<b>100.0%</b>	<b>3,935</b>	<b>100.0%</b>	<b>3,006</b>	<b>100.0%</b>
<b>GP/FM/DO<sup>†</sup></b>	<b>1,860</b>	<b>39.3%</b>	<b>1,548</b>	<b>39.3%</b>	<b>1,215</b>	<b>40.4%</b>
<b>Internal Medicine</b>	<b>1,734</b>	<b>36.6%</b>	<b>1,459</b>	<b>37.1%</b>	<b>1,137</b>	<b>37.8%</b>
<b>Cardiovascular Diseases</b>	<b>300</b>	<b>6.3%</b>	<b>252</b>	<b>6.4%</b>	<b>209</b>	<b>7.0%</b>
<b>Unspecified</b>	<b>369</b>	<b>7.8%</b>	<b>272</b>	<b>6.9%</b>	<b>116</b>	<b>3.8%</b>
<b>Nurse Practitioner</b>	<b>56</b>	<b>1.2%</b>	<b>51</b>	<b>1.3%</b>	<b>49</b>	<b>1.6%</b>
<b>Physician Assistant</b>	<b>44</b>	<b>0.9%</b>	<b>42</b>	<b>1.1%</b>	<b>36</b>	<b>1.2%</b>
<b>Endocrinology</b>	<b>43</b>	<b>0.9%</b>	<b>39</b>	<b>1.0%</b>	<b>33</b>	<b>1.1%</b>
<b>Pediatrics</b>	<b>36</b>	<b>0.8%</b>	<b>31</b>	<b>0.8%</b>	<b>25</b>	<b>0.8%</b>
<b>Hospital</b>	<b>34</b>	<b>0.7%</b>	<b>28</b>	<b>0.7%</b>	<b>23</b>	<b>0.8%</b>
<b>Pulmonary Disease</b>	<b>36</b>	<b>0.8%</b>	<b>28</b>	<b>0.7%</b>	<b>20</b>	<b>0.7%</b>
<b>Nephrology</b>	<b>27</b>	<b>0.6%</b>	<b>24</b>	<b>0.6%</b>	<b>19</b>	<b>0.6%</b>
<b>Geriatrics</b>	<b>20</b>	<b>0.4%</b>	<b>18</b>	<b>0.5%</b>	<b>15</b>	<b>0.5%</b>
<b>Emergency Medicaine</b>	<b>21</b>	<b>0.4%</b>	<b>18</b>	<b>0.5%</b>	<b>15</b>	<b>0.5%</b>
<b>Gastroenterology</b>	<b>21</b>	<b>0.4%</b>	<b>16</b>	<b>0.4%</b>	<b>12</b>	<b>0.4%</b>
<b>General Surgery</b>	<b>20</b>	<b>0.4%</b>	<b>15</b>	<b>0.4%</b>	<b>11</b>	<b>0.4%</b>
<b>Ob/Gyn</b>	<b>12</b>	<b>0.2%</b>	<b>10</b>	<b>0.2%</b>	<b>8</b>	<b>0.3%</b>
<b>Rheumatology</b>	<b>14</b>	<b>0.3%</b>	<b>10</b>	<b>0.3%</b>	<b>8</b>	<b>0.3%</b>
<b>Infectious Disease</b>	<b>12</b>	<b>0.3%</b>	<b>11</b>	<b>0.3%</b>	<b>7</b>	<b>0.2%</b>
<b>Oncology</b>	<b>8</b>	<b>0.2%</b>	<b>7</b>	<b>0.2%</b>	<b>5</b>	<b>0.2%</b>
<b>Other</b>	<b>9</b>	<b>0.2%</b>	<b>6</b>	<b>0.2%</b>	<b>5</b>	<b>0.2%</b>
<b>All Others</b>	<b>63</b>	<b>1.3%</b>	<b>50</b>	<b>1.3%</b>	<b>37</b>	<b>1.2%</b>

Verispan, LLC, Vector One<sup>®</sup> National (VONA) Data extracted 1-17-2007  
Source File: 2007-43 VONA 1-17-07 fluvastatin specialty 2004-2006.qry  
\*Numbers may not sum exactly, due to rounding  
<sup>†</sup>GP/FM/DO includes general practice, Family Medicine, Doctors of Osteopathy

### IV. Indication for Use

The most common indication for use of Lescol<sup>®</sup> or Lescol XL<sup>®</sup> (fluvastatin) for adult patients was “Disorder of Lipoid Metabolism” (ICD-9 272.0) which accounted for approximately 88% of adult Lescol<sup>®</sup> or Lescol XL<sup>®</sup> diagnosis mentions in both the pre and post-exclusivity periods (data not shown).<sup>4</sup> No indications for use were linked to patients aged 0-16 years during the study period.

<sup>4</sup> Verispan, LLC. Physician Drug and Diagnosis Audit, Extracted 1-12-07; File: 2007-43 PDDA 1-12-07 fluvastatin 3ddx 2004-2005 ytd 11-06.xls

## **DISCUSSION**

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Based on the databases employed for this analysis, the HMG-CoA reductase inhibitor class dominates the total cholesterol market share for dispensed prescriptions in the year 2006. Of the HMG-CoA reductase inhibitors, atorvastatin is the most commonly dispensed and fluvastatin is the least commonly dispensed, the latter representing approximately 3% of the HMG-CoA reductase inhibitor market share. The overall number of prescriptions dispensed for fluvastatin decreased by 24% from approximately 3.9 million prescriptions during the pre-exclusivity year of 2005 to approximately 3 million prescriptions during the post-exclusivity period. The share of dispensed fluvastatin prescriptions to the pediatric age group represented approximately 0.02% of the total dispensed prescriptions for fluvastatin during all three 1-year time periods (January 2004 to December 2006). There was a corresponding 24% decrease in the overall projected number of 723,956 unique patients in the pre-exclusivity period of January 2005 – December 2005 to 551,790 patients in the post exclusivity period. The pediatric population aged 0-16 years represented less than 1% of these patients.

Findings from this consult should be interpreted in the context of the known limitations of the databases used. We estimated that Lescol<sup>®</sup> and Lescol XL<sup>®</sup> are distributed primarily in outpatient settings based on the IMS Health, IMS National Sales Perspectives<sup>™</sup>. Mail order is the second most common retail distribution channel, accounting for up to 27% of wholesale sales. These data do not provide a direct estimate of use but do provide a national estimate of units sold from the manufacturer into the 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.

While we conducted a comprehensive analysis of the use of this product in the outpatient settings, in which the majority of use occurred, a significant proportion of wholesale sales of Lescol<sup>®</sup> and Lescol XL<sup>®</sup> was to mail order pharmacies, a distribution channel not currently captured by Verispan's retail prescription audits .

Verispan's Physician Drug & Diagnosis Audit (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 if use is not common in the pediatric population. Verispan recommends caution interpreting projected annual uses or mentions below 100,000 as the sample size is very small with correspondingly large confidence intervals.

## **CONCLUSION**

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In summary, there was an approximate 8% increase in the number of total dispensed prescriptions for marketed drugs in the HMG-CoA reductase inhibitor class (atorvastatin, lovastatin, pravastatin, simvastatin, rosuvastatin, and fluvastatin) during the 2005 to 2006 pre- and post-exclusivity time periods. The overall number of prescriptions dispensed for Lescol<sup>®</sup> and Lescol XL<sup>®</sup> (fluvastatin) , however, decreased for both the adult and pediatric populations. Pediatric patients accounted for less than 1% of the total dispensed prescriptions as well as unique patients during the entire study period.

General Practitice and Internal Medicine specialties were the most frequent prescribers of Lescol<sup>®</sup> and Lescol XL<sup>®</sup> (fluvastatin) and together accounted for over 75% of all dispensed prescriptions during the entire study period. The indication for use most frequently linked to Lescol<sup>®</sup> and Lescol XL<sup>®</sup> in adults was "Disorder of Lipoid Metabolism" (ICD-9 272.0). No indications for use were linked to pediatric patients during the study period.

## **APPENDIX**

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### ***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, mail order pharmacies, pharmacy benefits managers and their data systems, and provider groups. Vector One receives over 2 billion prescription claims, representing over 160 million unique patients.

Prescriptions are captured from a sample of approximately 54,000 pharmacies throughout the US. The pharmacies in the data base account for nearly all retail pharmacies and represent approximately 50% of 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.

### ***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 in the retail outpatient setting.

TPT derives its data from the Vector One database which integrates prescription activity from a variety of sources including national retail chains, mail order pharmacies, mass merchandisers, pharmacy benefits managers and their data systems. Vector one receives over 2 billion prescription claims per year, which represents over 160 million patients tracked across time.

### ***Verispan, LLC: Vector One: Verispan Concurrency (VOCON)***

Data used in VOCON is derived from Verispan's Vector One® database. The Vector One® database integrates prescription activity from a variety of sources, including national retail chains, mail order pharmacies, mass merchandisers, pharmacy benefits managers and their data systems, and provider groups. Vector One® receives over 2 billion prescription claims annually, representing over 160 million unique patients. Vector One receives approximately half the of retail prescriptions dispensed nationwide. Verispan obtains all prescriptions from approximately one-third of the reporting stores and a significant sample of prescriptions from the remaining stores.

VOCON allows users to measure and evaluate concurrent drug therapy usage in unique patients during a selected time period using four scenarios. These scenarios are (in order of most to least restrictive): Same day fills, overlapping days supply, overlapping days supply with % grace period, fills during the same time period.

The VOCON module provides unprojected patients counts. Nationwide projections are not available.

### ***Verispan, LLC: (Physician Drug & Diagnosis Audit ) PDDA***

Verispan's Physician Drug & Diagnosis Audit (PDDA) is a monthly survey designed to provide descriptive information on the patterns and treatment of diseases encountered in office-based physician practices in the U.S. The survey consists of data collected from 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.

***IMS Health: NSP Retail, Non-Retail or Combined (National Sales Perspective)***

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

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