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

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| Date: | January 29, 2008 |
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| Subject: | One Year Post-Pediatric Exclusivity Post-marketing Adverse Event Review:<br>Drug Utilization Analysis<br>Pediatric Exclusivity Grant Date: August 23, 2006 |
| Drug Name(s): | Colazal® (balsalazide) Capsules |
| Submission Number: | S-016 |
| Application Type/Number: | NDA 20-610 |
| Applicant/sponsor: | Salix Pharmaceuticals |
| OSE RCM #: | 2007-2198 |

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## EXECUTIVE SUMMARY

This review examines the drug utilization patterns for balsalazide (Colazal®), an anti-inflammatory agent used in the treatment of ulcerative colitis, two years before and one year following the granting of Pediatric Exclusivity on August 23, 2006, with a primary focus on the use in the pediatric population, ages 0 through 16 years. Outpatient drug use patterns for balsalazide, as well as other anti-inflammatory products used in the treatment of ulcerative colitis, were examined for the three 12-month periods from September 1, 2004 through August 31, 2007, using proprietary drug use databases licensed by FDA.

The total number of retail prescriptions dispensed for products used to treat ulcerative colitis has remained stable at approximately 4 million for the three 12-month periods from September 2004 to August 2007. Total retail prescriptions dispensed for balsalazide increased by nearly 4%, from approximately 299,878 prescriptions in the pre-exclusivity period (September 2005 –August 2006) to 311,535 prescriptions in the post-exclusivity period (September 2006 – August 2007).

Balsalazide is primarily used in adult patients. Patients aged 0-16 years comprise less than 3% of all patients that filled a prescription for balsalazide during the pre-exclusivity and post-exclusivity periods. Gastroenterology was the most common prescribing specialty for balsalazide, and pediatricians accounted for less than 2% of all dispensed prescriptions. Data from office-based physician practices in the U.S. indicates no recorded use of balsalazide within the pediatric population during the entire study period. Ulcerative colitis, noninfectious gastroenteritis, and regional enteritis were associated with a mention of balsalazide during adult patient visits (age 17 year and older).

# 1 BACKGROUND

## 1.1 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 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.

## 1.2 REGULATORY HISTORY

Colazal® (balsalazide disodium capsule) 750 mg, NDA 20-610, was approved on July 18, 2000 for the treatment of mild to moderate active ulcerative colitis. A supplemental new drug application, NDA 20-610/S-016 was approved on December 20, 2006 and provided for the use of Colazal (balsalazide disodium capsule) 750 mg for the treatment of mildly to moderately active ulcerative colitis in patients 5 years of age and older. Safety and effectiveness of Colazal beyond 8 weeks in children (ages 5-17 years) and 12 weeks in adults have not been established.

Pediatric exclusivity was granted on August 23, 2006. Pediatric use of Colazal was granted orphan drug status in December 2006 under FDA's Orphan Drug Program.

## 1.3 PRODUCT LABELING [1]

**2.2 Pediatric Dose**
For treatment of active ulcerative colitis in pediatric patients, aged 5 to 17 years, the usual dose is EITHER:
• three 750 mg COLAZAL capsules 3 times a day (6.75 g per day) for up to 8 weeks;
OR:
• one 750 mg COLAZAL capsule 3 times a day (2.25 g per day) for up to 8 weeks.
Use of COLAZAL in the pediatric population for more than 8 weeks has not been evaluated in clinical trials. *[See Clinical Studies Section (14)]*

**8.4 Pediatric Use**
A clinical trial of 68 patients ages 5-17 years has been conducted comparing two doses of COLAZAL (6.75 g/day and 2.25 g/day). [*see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14)]*. Based on the limited data available, dosing can be initiated at either 6.75 or 2.25 g/day.
Safety and efficacy of COLAZAL in pediatric patients below the age of 5 years have not been established.

# 2 METHODS AND MATERIALS

Using the currently available data resources, this review describes the outpatient drug use patterns for balsalazide in the pediatric population as well as in the adult population in the years prior to and subsequent to the granting of pediatric exclusivity on August 23, 2006. Proprietary drug use databases licensed by the Agency were used to conduct this analysis.

## 2.1 DETERMINING SETTINGS OF CARE

IMS Health, IMS National Sales Perspectives™ data were used to determine the settings in which balsalazide is sold. Sales of this product by extended units (number of capsules) sold from the manufacturer into the various retail and non-retail channels of distribution were analyzed for the year following the granting of pediatric exclusivity on August 23, 2006, from September 2006 through August 2007. Based on these data, balsalazide is primarily distributed to the outpatient setting. Nearly 96% of the balsalazide extended units (capsules) were sold to retail sales channels (which include 24% of sales to mail service pharmacies), and approximately 4% were sold to inpatient settings of care (Table 1).

[1] Drugs@FDA. http://www.fda.gov/cder/foi/label/2007/020610s017lbl.pdf

**Table 1: Projected number of total extended units (capsules) of Colazal (in thousands) sold from the manufacturer to retail and non-retail pharmacies in the U.S., moving annual totals September 2004 through August 2007**

| | September 2004 - August 2005 | | September 2005 - August 2006 | | September 2006 - August 2007 | |
|---|---|---|---|---|---|---|
| Colazal® | Extended Units N (000) | *Share* % | Extended Units N (000) | *Share* % | Extended Units N (000) | *Share* % |
| **Total** | 95,526 | *100.0* | 103,626 | *100.0* | 108,422 | *100.0* |
| **Retail** | 91,755 | *96.0* | 99,289 | *95.9* | 103,567 | *95.5* |
| **Mail Order** | 21,723 | *22.7* | 24,101 | *23.3* | 26,142 | *24.1* |
| **Non-Retail** | 3,771 | *3.9* | 4,337 | *4.0* | 4,856 | *4.4* |

IMS HEALTH, IMS National Sales PerspectiveTM, September 2004 - August 2007, Data extracted 10-2007. Source File: NSPC 2007-2198 BPCA Colazal 10-23-07 0710bals.dvr
Retail Channels: Food Stores, Chain Pharmacies, Independent Pharmacies, Mail Order Pharmacies.
Non-Retail Channels: Long Term Care Facilities, Clinics, Non-Federal Hospitals, Prisons, Federal Facilities, Home Health Care, HMOs, Universities.

### 2.2 DATA SOURCES USED

Outpatient use and patient demographics were measured with two data sources from Verispan, LLC: Vector One®: National (VONA) and Total Patient Tracker (TPT) (see Appendix). From these two sources, nationally projected estimates of the number of prescriptions dispensed by retail pharmacies and the number of patients who received a dispensed prescription for Colazal® (balsalazide) were obtained. Indications for use were obtained from the Verispan, Physician Drug and Diagnosis Audit database (see Appendix). Outpatient drug utilization patterns were examined for three twelve-month periods from September 1, 2004 through August 31, 2007.

### 2.3 PRODUCTS INCLUDED

We examined prescriptions dispensed for Colazal® (balsalazide), mesalamine, sulfasalazine, and olsalazine, which are all anti-inflammatory products used in the treatment of ulcerative colitis, based upon discussions with the Pediatric and Maternal Health Staff.

## 3 RESULTS

### 3.1 DISPENSED PRESCRIPTIONS

**Table 2. Projected number of retail prescriptions for medications used to treat ulcerative colitis dispensed from U.S. retail pharmacies, Moving Annual Totals September 2004 through August 2007**

| | September 2004- August 2005 | | September 2005- August 2006 | | September 2006- August 2007 | |
|---|---|---|---|---|---|---|
| | Retail Rxs | *Share* | Retail Rxs | *Share* | Retail Rxs | *Share* |
| | N | *%* | N | *%* | N | *%* |
| **Total** | 4,019,784 | *100.0%* | 3,987,310 | *100.0%* | 4,070,702 | *100.0%* |
| **mesalamine** | 2,534,288 | *63.0%* | 2,518,895 | *63.2%* | 2,614,215 | *64.2%* |
| **sulfasalazine** | 1,148,861 | *28.6%* | 1,121,136 | *28.1%* | 1,104,100 | *27.1%* |
| **balsalazide** | 281,998 | *7.0%* | 299,878 | *7.5%* | 311,535 | *7.7%* |
| **olsalazine** | 54,637 | *1.4%* | 47,401 | *1.2%* | 40,852 | *1.0%* |

Verispan Vector One®: National (VONA), Data extracted 10-2007.
Source File: 2007-2198 10-19-07 balsalazide comp 10-19-07.qry

### *3.1.1 Anti-Inflammatory Products*

The total number of retail prescriptions dispensed for products used to treat ulcerative colitis has remained stable at approximately 4 million for the three 12-month periods from September 2004 to August 2007 (Table 2 and Appendix 2, Figure 1). Mesalamine held the largest market share at an average 63.5% during this time period. Dispensed prescriptions for balsalazide accounted for approximately 7-8% of the market share among these agents used to treat ulcerative colitis.

### *3.1.2 Balsalazide*

Total retail prescriptions dispensed for balsalazide increased by nearly 4%, from approximately 299,878 prescriptions in the pre-exclusivity period (September 2005 –August 2006) to 311,535 prescriptions in the post-exclusivity period (September 2006 – August 2007) (Table 2 and Appendix 2, Figure 1). Over 10% increase in prescription volume occurred from September 2004 –August 2005 to September 2006 – August 2007, when the number of prescriptions dispensed for balsalazide rose from approximately 281,998 prescriptions to 311,535 prescriptions.

## 3.2 PATIENT DEMOGRAPHICS

### *3.2.1 Prescriptions Dispensed*

#### 3.2.1.1 Anti-Inflammatory Products

Examination of the other anti-inflammatory products used in the treatment of ulcerative colitis revealed that more prescriptions for pediatric patients aged 0-16 years were filled for mesalamine products during each of the three 12-month periods from September 2004 to August 2007. However, the percentage of retail prescriptions dispensed to pediatric patients aged 0-16 years was the same for meslamine and olsalazine prescriptions, accounting for approximately 3.2% of the total number of prescriptions dispensed for each product during the post-exclusivity period (Table 3, Appendix 2, Figure 2).

**Table 3. Projected number of retail prescriptions for medications used to treat ulcerative colitis dispensed to pediatric patients aged 0-16 years, Moving Annual Totals September 2004 through August 2007**

| | September 2004- August 2005 | | | | | September 2005- August 2006 | | | | September 2006 - August 2007 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total Rxs | *Share* | Retail Rxs | *Share* | Mail Rxs | Total Rxs | Retail Rxs | *Share* | Mail Rxs | Total Rxs | Retail Rxs | *Share* | Mail Rxs |
| | N | *%* | N | *%* | N | N | N | *%* | N | N | N | % | N |
| **mesalamine** | Not Available | | **84,489** | **3.4%** | Not Available | **87,586** | **79,909** | ***3.2%*** | **7,677** | **90,100** | **82,774** | **3.2%** | **7,326** |
| **sulfasalazine** | | | **27,184** | ***2.3%*** | | **27,160** | **26,071** | ***2.4%*** | **1,089** | **26,985** | **26,147** | **2.4%** | **838** |
| **balsalazide** | | | **6,879** | ***2.4%*** | | **8,577** | **7,814** | ***2.6%*** | **763** | **9,255** | **8,528** | **2.7%** | **727** |
| **olsalazine** | | | **2,137** | ***3.8%*** | | **1,903** | **1,809** | ***3.8%*** | **94** | **1,332** | **1,279** | **3.2%** | **53** |

Verispan Vector One®: National, Data extracted 10-2007.
Source File: 2007-2198 10-19-07 balsalazide age 10-19-07.qry

### 3.2.1.2 Balsalazide

Balsalazide is primarily used in adult patients. Prescriptions dispensed to pediatric patients (ages 0-16 years) accounted for less than 3% of total retail dispensed prescriptions for balsalazide during the time period studied in this analysis. The majority of prescriptions dispensed to pediatric patients for balsalazide were for patients aged 11-16 years, accounting for nearly 2% of total dispensed prescriptions for balsalazide (Table 4).

**Table 4. Projected number of retail prescriptions, by age, for balsalazide dispensed from U.S. retail pharmacies, Moving Annual Totals September 2004 through August 2007**

| | September 2004- August 2005 | | | | | September 2005 - August 2006 | | | | September 2006 - August 2007 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total Rxs | *Share* | Retail Rxs | *Share* | Mail Rxs | Total Rxs | *Retail Rxs* | Share | Mail Rxs | Total Rxs | *Retail Rxs* | Share | Mail Rxs |
| | N | *%* | N | *%* | N | N | *N* | % | N | N | *N* | % | N |
| **balsalazide** | | | 281,998 | 7.0% | | 342,636 | 299878 | *100%* | 42,758 | 356,738 | 311535 | *100%* | 45,203 |
| **0-16** | | | **6,879** | ***2.4%*** | | **8,577** | ***7814*** | ***2.6%*** | **763** | **9,255** | ***8528*** | ***2.7%*** | **727** |
| **0-1** | | | 9 | 0.0% | | 7 | 7 | *0.0%* | -- | 44 | 36 | *0.0%* | 8 |
| **2-5** | | | 330 | 0.1% | | 397 | 376 | *0.1%* | 21 | 505 | 467 | *0.1%* | 38 |
| **6-10** | | | 1,466 | 0.5% | | 1,906 | 1784 | *0.6%* | 122 | 2,024 | 1941 | *0.6%* | 83 |
| **11-16** | | | 5,074 | 1.8% | | 6,267 | 5647 | *1.9%* | 620 | 6,682 | 6084 | *2.0%* | 598 |
| ***17+*** | Not Available | | 274,140 | 97.2% | Not Available | 333,146 | 291156 | *97.1%* | 41,990 | 347,011 | 302538 | *97.1%* | 44,473 |
| **UNSPEC.** | | | 979 | 0.3% | | 913 | 908 | *0.3%* | 5 | 472 | 469 | *0.2%* | 3 |

Verispan Vector One®: National, Data extracted 10-2007. Source File: 2007-2198 10-19-07 balsalazide age 10-19-07.qry

## *3.2.2 Patient Counts for Dispensed Prescriptions*

### 3.2.2.1 Anti-Inflammatory Products

In terms of the number of unique patients exposed, Dipentum® (olsalazine) was the product with the highest percentage of use in pediatric patients aged 0-16 years with approximately 4% in the pre-exclusivity period (September 2005 –August 2006) and over 3% in the post-exclusivity period (September 2006 – August 2007) (Appendix 2, Table 7 and Figure 3). Similar to dispensed prescription data, however, mesalamine was dispensed to the largest number of pediatric patients. During the entire time period examined, pediatric patients accounted for approximately 3% of use for Colazal® (balsalazide), mesalamine products as a group, and sulfasalazine products. The majority of pediatric exposure went to patients aged 11-16 years for all these products.

### 3.2.2.2 Balsalazide

Trends for patient data were similar to that of prescription data. The number of patients receiving a prescription for balsalazide from outpatient retail pharmacies slightly increased by 1%, from approximately 73,341 patients in the pre-exclusivity period (September 2005 –August 2006) to 74,399 patients in the post-exclusivity period (September 2006 – August 2007) (Table 5). Approximately 3% of those patients were pediatrics aged 0-16 years. The number of pediatric patients receiving a prescription for balsalazide increased by 5%, from approximately 2,046 patients in the pre-exclusivity period (September 2005 –August 2006) to 2,143 patients in the post-exclusivity period (September 2006 – August 2007) (Table 5). Patients aged 11-16 years filled the majority of the prescriptions written for pediatric patients.

**Table 5: Total number of patients* receiving a prescription for Colazal®, in outpatient retail pharmacies by patient age, Moving Annual Total September 2004 through August 2007 (mail order pharmacies not included)**

| | September 2004- August 2005 | | September 2005- August 2006 | | September 2006- August 2007 | |
|---|---|---|---|---|---|---|
| | **Projected Patient Count** | ***Share %*** | **Projected Patient Count** | ***Share %*** | **Projected Patient Count** | ***Share %*** |
| **Colazal®** | **69,012** | ***100.00%*** | **73,341** | ***100.00%*** | **74,399** | ***100.00%*** |
| **0-16** | **1,734** | ***2.51%*** | **2,046** | ***2.76%*** | **2,143** | ***2.97%*** |
| **0 - 2** | 16 | *0.02%* | 21 | *0.03%* | 35 | *0.05%* |
| **3 - 5** | 106 | *0.15%* | 108 | *0.15%* | 162 | *0.22%* |
| **6 - 10** | 343 | *0.50%* | 419 | *0.56%* | 457 | *0.63%* |
| **11 - 16** | 1,314 | *1.90%* | 1,543 | *2.08%* | 1,565 | *2.17%* |
| **17+** | **67,126** | ***97.18%*** | **71,912** | ***97.00%*** | **69,949** | ***97.00%*** |
| **Unknown Age** | 701 | *1.02%* | 714 | *0.97%* | 563 | *0.76%* |

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

Source: Verispan, LLC: Total Patient Tracker, September 2004 -August 2007, Extracted Sept07. File: TPT 2007-2198 Colazal BPCA 10-23-07.xls

## 3.3 PRESCRIBER SPECIALTY

Gastroentrology was the most common prescribing specialty for balsalazide, accounting for approximately 70% of the dispensed retail prescriptions during each year of the study period (Table 6). Internal Medicine was the second most common prescribing specialty, with approximately 10% of the retail dispensed prescriptions. Prescriptions by pediatricians accounted for an average 2% of all retail dispensed prescriptions for balsalazide during the three 12-month periods of this analysis.

**Table 6: Total number of prescriptions dispensed for Balsalzide by top 10 prescriber specialties, Moving Annual Total September 2004 through August 2007**

| | MAT/AUG/2005 | | | | | MAT/AUG/2006 | | | | MAT/AUG/2007 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total Rxs | *Share* | Retail Rxs | *Share* | Mail Rxs | Total Rxs | Retail Rxs | *Share* | Mail Rxs | Total Rxs | Retail Rxs | *Share* | Mail Rxs |
| | N | *%* | N | *%* | N | N | N | *%* | N | N | N | *%* | N |
| **TOTAL** | | | **281,995** | ***100.0%*** | | **342,648** | **299,875** | ***100.0%*** | **42,773** | **356,755** | **311,524** | ***100.0%*** | **45,231** |
| **GE** | | | 198,575 | *70.4%* | | 241,784 | 210,346 | *70.1%* | 31,438 | 247,963 | 216,848 | *69.6%* | 31,115 |
| **IM** | | | 26,729 | *9.5%* | | 34,081 | 29,502 | *9.8%* | 4,579 | 35,744 | 30,725 | *9.9%* | 5,019 |
| **UNSPEC** | | | 19,953 | *7.1%* | | 19,051 | 16,955 | *5.7%* | 2,096 | 17,901 | 14,298 | *4.6%* | 3,603 |
| **GP/FM/DO** | | | 8,852 | *3.1%* | | 12,643 | 11,027 | *3.7%* | 1,616 | 14,259 | 12,538 | *4.0%* | 1,721 |
| **PED** | | | **5,106** | ***1.8%*** | | **7,567** | **6,800** | ***2.3%*** | **767** | **9,051** | **8,201** | ***2.6%*** | **850** |
| **AO SURG** | | | 4,882 | *1.7%* | | 5,797 | 5,274 | *1.8%* | 523 | 6,447 | 5,814 | *1.9%* | 633 |
| **NP** | | | 2,725 | *1.0%* | | 4,130 | 3,677 | *1.2%* | 453 | 5,942 | 5,210 | *1.7%* | 732 |
| **HOSP** | | | 4,992 | *1.8%* | | 5,408 | 5,345 | *1.8%* | 63 | 4,959 | 4,914 | *1.6%* | 45 |
| **PA** | | | 1,753 | *0.6%* | | 2,769 | 2,464 | *0.8%* | 305 | 3,613 | 3,233 | *1.0%* | 380 |
| **GEN SURG** | | | 1,673 | *0.6%* | | 2,152 | 1,904 | *0.6%* | 248 | 2,432 | 2,164 | *0.7%* | 268 |
| **All Others** | | | 6,755 | *2.4%* | | 7,266 | 6,581 | *2.2%* | 685 | 8,444 | 7,579 | *2.4%* | 865 |

Not Available (Share) | Not Available (Mail Rxs)

Verispan Vector One®: Prescription Services, Data extracted 10-2007. Source File: 2007-2198 balsalazide MD 10-19-07.qry

### 3.4 INDICATIONS FOR USE

Based on data obtained from Verispan's office-based physician practice survey database, no mention of balsalazide in association with a pediatric visit was recorded during the entire period from September 2004 – August 2007 (data not shown)[2]. The following diagnoses associated with the use of balsalazide in adults were recorded during the pre-exclusivity period: "ulcerative colitis" (ICD-9 556.9), "noninfectious gastroenteritis" (ICD-9 558.9), and "regional enteritis" (ICD-9 555.9).

## 4 DISCUSSION

Based on the databases employed for this analysis, prescriptions dispensed for Colazal® in the pediatric population accounted for only small proportion of the total prescriptions for balsalazide as well as other anti-inflammatory products used for the treatment of ulcerative colitis during the pre- and post-exclusivity periods.

Findings from this review should be interpreted in the context of the known limitations of the databases used. We estimated that balsalazide is distributed primarily in outpatient settings based on the IMS Health, IMS 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 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 setting, in which the majority of use occurred, a significant proportion of wholesale sales of balsalazide products were to mail order pharmacies. Verispan's mail order data begins January 2005, and mail order data from the date onward was included in this analysis.

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

[2] Source File: PDDA 2007-2198 colazal diag 10-19-07.xls

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 and trending variability. For instance, the diagnoses associated with the use of balsalazide should be viewed without regard to extent of use.

## 5 CONCLUSIONS

In the most recent 12-months of this analysis, approximately 3% of prescriptions dispensed for balsalazide are for pediatric patients. Gastroenterology was the most common prescribing specialty for balsalazide at 70%, followed by Internal Medicine at 10%. Prescriptions by pediatricians accounted for an average 2% of all dispensed prescriptions for balsalazide during the time period examined. Examining product usage by diagnosis, there were no mentions associated with balsalazide in the pediatric population; however, the most commonly mentioned indication associated with balsalazide in the adult population was “ulcerative colitis” during the entire study period.

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## APPENDICES

### *APPENDIX 1: Database Descriptions*

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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 1.5 billion prescription claims per year, representing over 100 million unique patients. Since 2002 Vector One® has captured information on over 8 billion prescriptions representing 200 million unique patients.

Prescriptions are captured from a sample of approximately 59,000 pharmacies throughout the US. The pharmacies in the data base account for nearly all retail pharmacies and represent nearly half 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®: Mail Order (VOMA)*

Verispan's VOMA measures mail order dispensing of prescriptions or the frequency with which drugs move out of mail order pharmacies into the hands of consumers via formal prescriptions. Information on the number of prescriptions, extended units, patient age and gender, acquisition cost, prescription size and prescriptions per physician is available.

The Vector One® Mail Order data are collected directly from contracted mail order pharmacies which provide data for every prescription dispensed. Verispan's Mail Order sample contains approximately 25% of all mail order prescriptions dispensed in the U.S. Data are received from approximately 140 mail order stores out of a 250 store universe, and are obtained from both Medco and non-Medco sources.

Verispan captures roughly 5 million raw scripts which are projected to a national total of mail order activity of 20 million prescriptions.

#### *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: 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.

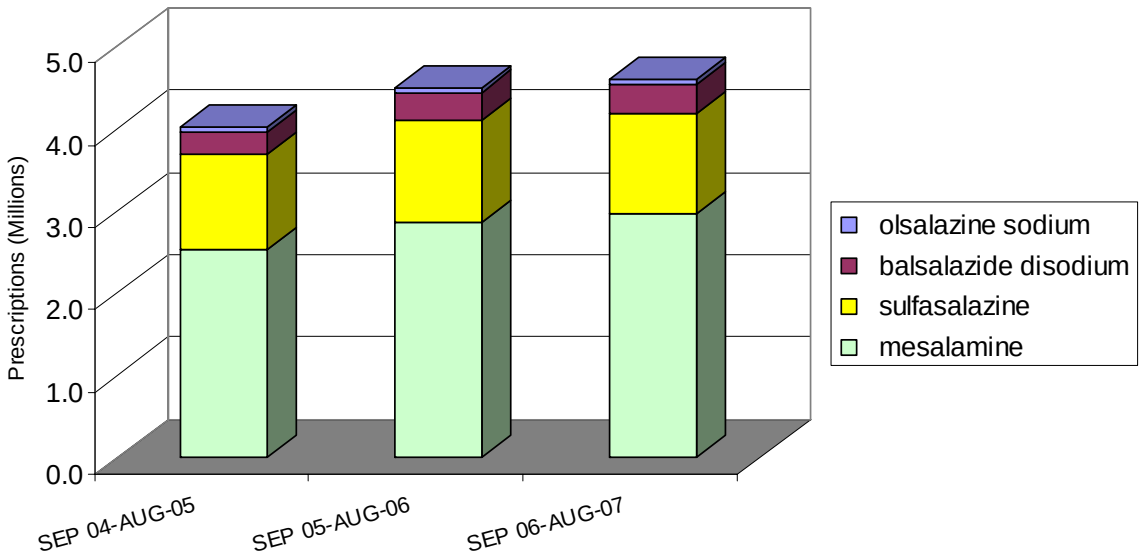
### *IMS Health, IMS National Sales Perspectives™: Retail and Non-Retail*

The 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. Volume is expressed in terms of sales dollars, eaches, extended units, and share of market. These data are based on national projections. 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.

*APPENDIX 2: Charts and Figures*

**Figure 1. Projected number of retail prescriptions for medications used to treat ulcerative colitis dispensed from U.S. retail pharmacies, September 2004 through August 2007**

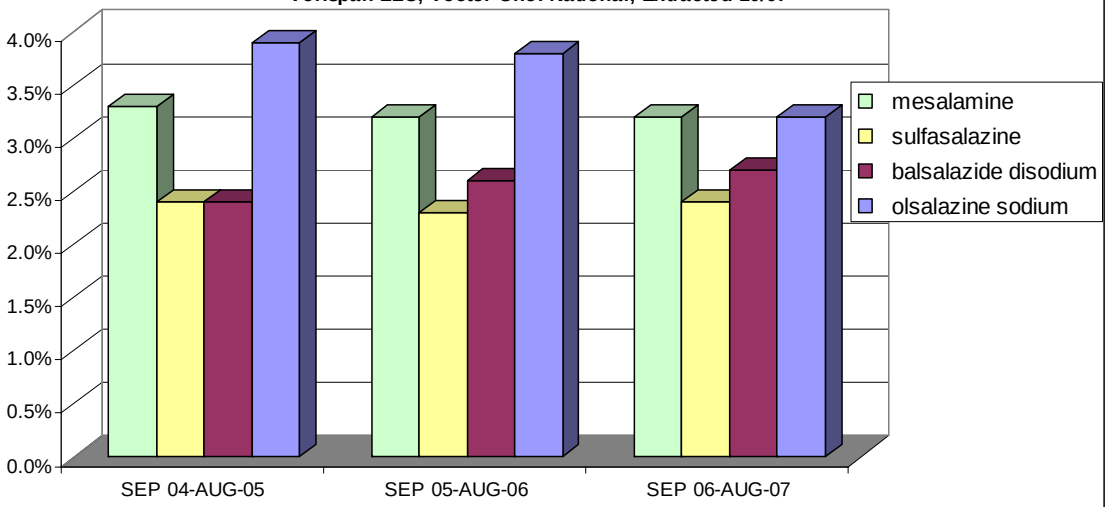
**Verispan LLC, Vector One: Prescription Services, Extracted 10/07**




Source File: VONA 2007-2198 balsalazide comp 10-19-07.xls

**Figure 2: Percentage of prescriptions for medications used to treat ulcerative colitis dispensed to pediatric patients aged 0-16 years from U.S. retail pharmacies, September 2004 through August 2007**

**Verispan LLC, Vector One: National, Extracted 10/07**



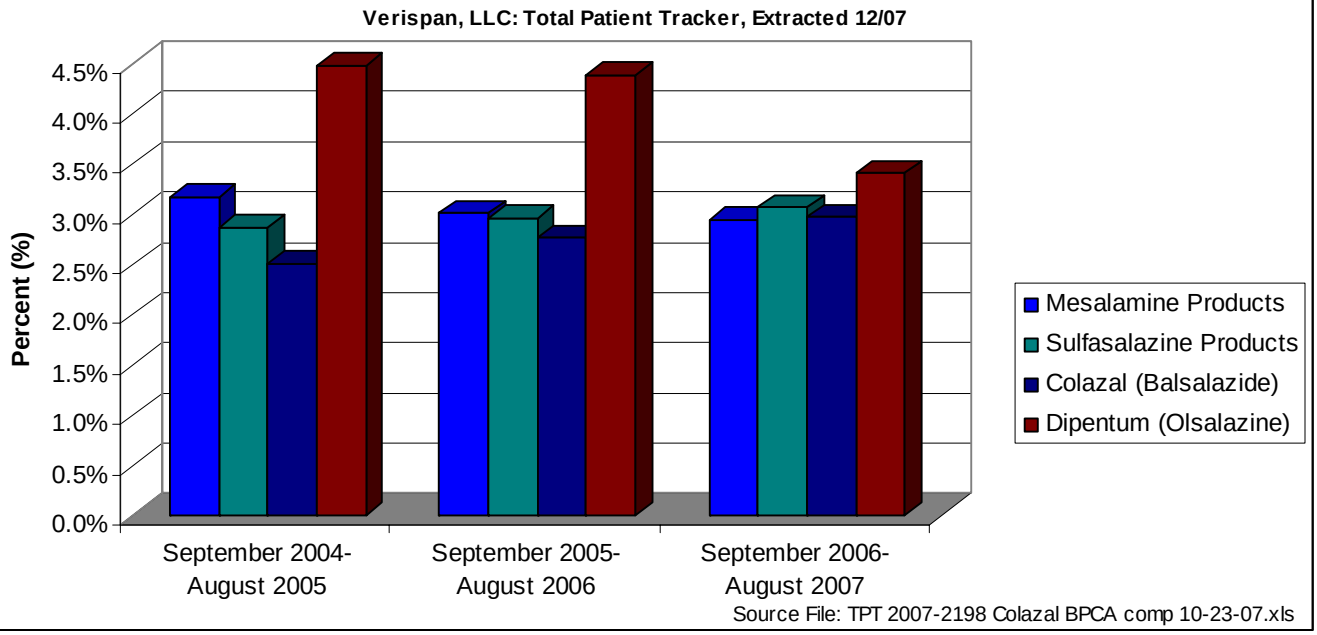

Source File: VONA 2007-2198 balsalazide comp 10-19-07.xls

**Table 7: Total number of patients*, by age, receiving a prescription for ulcerative colitis products, in outpatient retail pharmacies, Moving Annual Total September 2004 through August 2007 (mail order pharmacies not included)**

| | September 2004- August 2005 | | September 2005- August 2006 | | September 2006- August 2007 | |
|---|---|---|---|---|---|---|
| | Projected Patient Count | *Share %* | Projected Patient Count | *Share %* | Projected Patient Count | *Share %* |
| **Mesalamine Products** | **604,014** | **100.00%** | **610,078** | **100.00%** | **615,936** | **100.00%** |
| **0 - 16** | **19,161** | **3.17%** | **18,343** | **3.01%** | **18,129** | **2.94%** |
| **0 - 2** | 284 | 0.05% | 216 | 0.04% | 191 | 0.03% |
| **3 - 5** | 758 | 0.13% | 638 | 0.10% | 657 | 0.11% |
| **6 - 10** | 3,332 | 0.55% | 3,219 | 0.53% | 3,358 | 0.55% |
| **11 - 16** | 15,373 | 2.55% | 14,768 | 2.42% | 14,443 | 2.34% |
| **17+** | **581,460** | **96.27%** | **589,711** | **96.66%** | **597,101** | **96.94%** |
| **UNKNOWN AGE** | 11,124 | 1.84% | 8,542 | 1.40% | 7,185 | 1.17% |
| **Sulfasalazine Products** | **259,982** | **100.00%** | **261,151** | **100.00%** | **250,883** | **100.00%** |
| **0 - 16** | **7,457** | **2.87%** | **7,748** | **2.97%** | **7,688** | **3.06%** |
| **0 - 2** | 480 | 0.18% | 672 | 0.26% | 856 | 0.34% |
| **3 - 5** | 1,630 | 0.63% | 1,411 | 0.54% | 895 | 0.36% |
| **6 - 10** | 1,923 | 0.74% | 2,438 | 0.93% | 2,902 | 1.16% |
| **11 - 16** | 3,809 | 1.46% | 3,672 | 1.41% | 3,434 | 1.37% |
| **17+** | **250,604** | **96.39%** | **252,046** | **96.51%** | **242,444** | **96.64%** |
| **UNKNOWN AGE** | 5,765 | 2.22% | 4,835 | 1.85% | 3,891 | 1.55% |
| **Colazal (Balsalazide)** | **69,012** | **100.00%** | **73,341** | **100.00%** | **74,399** | **100.00%** |
| **0 - 16** | **1,734** | **2.51%** | **2,046** | **2.76%** | **2,143** | **2.97%** |
| **0 - 2** | 16 | 0.02% | 21 | 0.03% | 35 | 0.05% |
| **3 - 5** | 106 | 0.15% | 108 | 0.15% | 162 | 0.22% |
| **6 - 10** | 343 | 0.50% | 419 | 0.56% | 457 | 0.63% |
| **11 - 16** | 1,314 | 1.90% | 1,543 | 2.08% | 1,565 | 2.17% |
| **17+** | **67,126** | **97.18%** | **71,912** | **97.00%** | **69,949** | **97.00%** |
| **UNKNOWN AGE** | 701 | 1.02% | 714 | 0.97% | 563 | 0.76% |
| **Dipentum (Olsalazine)** | **11,786** | **100.00%** | **10,252** | **100.00%** | **8,262** | **100.00%** |
| **0 - 16** | **527** | **4.47%** | **449** | **4.38%** | **281** | **3.41%** |
| **0 - 2** | 19 | 0.16% | 25 | 0.24% | 8 | 0.10% |
| **3 - 5** | 77 | 0.65% | 52 | 0.51% | 33 | 0.40% |
| **6 - 10** | 127 | 1.08% | 114 | 1.11% | 81 | 0.98% |
| **11 - 16** | 321 | 2.72% | 278 | 2.72% | 175 | 2.11% |
| **17+** | **11,175** | **94.82%** | **9,747** | **95.08%** | **7,962** | **96.37%** |
| **UNKNOWN AGE** | 302 | 2.56% | 234 | 2.28% | 173 | 2.09% |

*Subtotals may not sum exactly, due to rounding. 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. Source: Verispan, LLC: Total Patient Tracker, September 2004 -August 2007, Extracted December07. File: TPT 2007-2198 Colazal BPCA comp 10-23-07.xls

**Figure 3: Percentage of pediatric patients aged 0-16 years that filled a prescription for the treatment of ulcerative colitis in U.S. Retail pharmacies, September 2004 through August 2007**




Source File: TPT 2007-2198 Colazal BPCA comp 10-23-07.xls

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/s/
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Kendra Worthy
1/30/2008 10:41:27 AM
DRUG SAFETY OFFICE REVIEWER

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