

Memorandum

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Center for Drug Evaluation and Research

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TO: M. Dianne Murphy, MD
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SUBJECT: Post-Pediatric Exclusivity Post-marketing Adverse Event Review: Drug Use Data Update
Oxybutynin (Ditropan[®] NDAs 17-577 and 18-211, Ditropan XL[®]; NDA 20-897,
Oxytrol[®]; NDA 21-351, multiple oxybutynin immediate release generic products)
Pediatric Exclusivity Granted Date: February 8, 2002

****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.****

Introduction

On June 12, 2003, the Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committee was presented the 1 year post-exclusivity adverse event review mandated by BPCA for Ditropan[®] (oxybutynin), which was granted exclusivity on February 3, 2002. Due to the small number of reports available in the year after the granting of exclusivity, the committee requested follow-up review in one year. In September, 2006, adverse event data were provided to the committee with a resultant request for another follow-up at the March, 2007 meeting.

This summary review provides a drug use data update for the use of oxybutynin products (Ditropan[®], Ditropan[®] XL, generic oxybutynin and Oxytrol[®] patches with a focus on data from 2006 and the use of Ditropan[®] XL and Oxytrol[®] in the pediatric population. The detailed drug use spreadsheets which were used to write this review are available from the OSE Drug Use Evaluation Team.

Data for this request were obtained from 3 sources. Outpatient dispensed prescriptions for retail pharmacies (excluding mail order) were obtained from Verispan Vector One[®]: National. Counts of unique patients receiving oxybutynin products through retail pharmacies (excluding mail order) were obtained from Verispan Vector One[®]: Total Patient Tracker. The indication for use of oxybutynin products was obtained using Verispan's Physician Drug and Diagnosis Audit. All data were obtained at the generic drug (molecule) and product levels from 2002 through 2006 and were stratified by the patient age bands (in years) requested by DDRE (0-5, 6-16, 17-29, 20-39, 40-59, 60-69, 79-79, 80+).

Summary of Oxybutynin Drug Usage

- The wholesale sales of oxybutynin products are primarily into the retail channels of distribution. Between 62%-67% of sales were into the retail distribution channels (chain, food store, independent pharmacies) for each year from 2002 through 2006 (Table 1). The sales into mail order pharmacies climbed from 15% in 2002 to 19% in 2006¹.
- The total number prescriptions dispensed through retail pharmacies (mail order excluded) for all oxybutynin products rose from 5.4 million in 2002 to 5.7 million in 2004 before declining to 4.9 million in 2006 (table 2).
- Ditropan[®] XL was the most commonly dispensed product from 2002 through 2005 (Table 3). However, its market share declined from 59% in 2002 to 43% in 2006. Generic oxybutynin was the second most commonly dispensed product from 2002 (41% of dispensed prescriptions) through 2005, but became the most commonly dispensed product during 2006 (50% of dispensed prescriptions).
- Pediatric patients age 0-5 years accounted for 0.7%-0.8% of yearly oxybutynin prescriptions, while patients age 6-16 years accounted for approximately 4% of yearly prescriptions (Table 3).
- Pediatric patients age 0-5 years were more likely to receive immediate release oxybutynin products². During 2006, approximately 95% of oxybutynin prescriptions dispensed to these patients were for an immediate release form, 4.97% were for Ditropan[®] XL, and 2.5% were Oxytrol[®] patches.
- Approximately 18 thousand patients 0-5 years of age (1.55% of total) received a prescription for any oxybutynin product during 2006, an overall decline from 22 thousand in 2002 (1.6% of total) (table 4).
- During 2006, Ditropan[®] XL was dispensed to approximately 700 patients age 0-5 years (0.15% of Ditropan[®] XL patients) while Oxytrol[®] was dispensed to approximately 400 patients age 0-5 years (0.43% of Oxytrol[®] patients) (Table 5).
- From 2002 through 2006, office based physician mentioned indications for use of oxybutynin in patients age 0-5 years of age were frequency of urination/polyuria, male hypospadias, incontinence of urine, bladder disorder, spina bifida and bladder dysfunction. Due to the low use of these products in this age band and the small sample size, determining the most common diagnoses are impossible. For all other patient age bands, the two most commonly mentioned indications for use of oxybutynin were incontinence of urine and bladder dysfunction³.

¹ IMS Health, IMS National Sales Perspectives combinedTM, Extracted 2-1-07. source file: 0702oxyb.dvr

² Verispan Vector One: National, extracted 1-2007, file: VONA Gish 1-26-07 2007-181 Oxybutynin.xls, Data table not shown

³ Verispan Physician Drug and Diagnosis Audit, extracted 1-2007. File: PDDA Gish 1-30-07 2007-181 Oxybutynin.xls Data table not shown

Methods and Materials - Database Descriptions

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

The IMS Health, 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.

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: (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.

Data / Results

Table 1. Total Extended Units (Tablets/Patches) of Oxybutynin Products Sold in the U.S. from 2002 – 2006, Stratified by distribution Channel

| | 2002 | | 2003 | | 2004 | | 2005 | | 2006 | |
|-------------------|----------------------|-------|----------------------|-------|----------------------|-------|----------------------|-------|----------------------|-------|
| | Extended Units (000) | Share |
| Oxybutynin | 417,236 | 100% | 449,702 | 100% | 430,863 | 100% | 422,370 | 100% | 412,865 | 100% |
| Retail | 277,450 | 67% | 286,717 | 64% | 266,978 | 62% | 260,086 | 62% | 257,119 | 62% |
| Mail Order | 62,721 | 15% | 69,984 | 16% | 83,297 | 19% | 81,252 | 19% | 78,952 | 19% |
| Non-Retail | 77,063 | 18% | 93,001 | 21% | 80,588 | 19% | 81,033 | 19% | 76,794 | 19% |

IMS Health, IMS National Sales Perspectives™, Extracted 2-1-07. source file: 0702oxyb.dvr

Retail channels: Independent, chain, and food store pharmacies

Non-Retail Channels: long term care, federal facilities, clinics, non-federal hospitals, homes, home health care, miscellaneous

Table 2. Total Oxybutynin Prescriptions Dispensed Through Retail Pharmacies in the U.S. from 2002 through 2006, by Patient Age (years)

| | 2002 | | 2003 | | 2004 | | 2005 | | 2006 | |
|--------------------|------------|---------|------------|---------|------------|---------|------------|---------|------------|---------|
| | TRxs (000) | Share % |
| Oxybutynin | 5,373 | 100.0% | 5,589 | 100.0% | 5,741 | 100.0% | 5,237 | 100.0% | 4,881 | 100.0% |
| Ditropan XL | 3,152 | 58.7% | 3,309 | 59.2% | 3,136 | 54.6% | 2,645 | 50.5% | 2,097 | 43.0% |
| Oxybutynin | 2,185 | 40.7% | 2,135 | 38.2% | 2,168 | 37.8% | 2,216 | 42.3% | 2,463 | 50.5% |
| Ditropan | 36 | 0.7% | 23 | 0.4% | 16 | 0.3% | 12 | 0.2% | 9 | 0.2% |
| Oxytrol | -- | -- | 122 | 2.2% | 422 | 7.4% | 364 | 7.0% | 312 | 6.4% |

Verispan Vector One: National, Data Extracted 2-1-06. File: VONA 1-26-07 2007-181 Oxybutynin.xls

Table 3. Total Oxybutynin Prescriptions Dispensed Through Retail Pharmacies in the U.S. from 2002 through 2006, by Patient Age (years)

| | 2002 | | 2003 | | 2004 | | 2005 | | 2006 | |
|-------------------|------------|---------|------------|---------|------------|---------|------------|---------|------------|---------|
| | TRxs (000) | Share % |
| Oxybutynin | 5,373 | 100.00% | 5,589 | 100.00% | 5,741 | 100.00% | 5,237 | 100.00% | 4,881 | 100.00% |
| 0-5 | 44 | 0.82% | 44 | 0.78% | 40 | 0.70% | 35 | 0.66% | 38 | 0.77% |
| 6-16 | 223 | 4.14% | 221 | 3.96% | 215 | 3.74% | 199 | 3.80% | 203 | 4.16% |
| 17-29 | 150 | 2.80% | 157 | 2.82% | 157 | 2.73% | 144 | 2.75% | 136 | 2.78% |
| 30-39 | 238 | 4.42% | 240 | 4.29% | 224 | 3.90% | 195 | 3.72% | 187 | 3.83% |
| 40-59 | 1,434 | 26.68% | 1,483 | 26.53% | 1,466 | 25.54% | 1,331 | 25.41% | 1,240 | 25.41% |
| 60-69 | 853 | 15.87% | 916 | 16.40% | 937 | 16.32% | 865 | 16.53% | 859 | 17.59% |
| 70-79 | 1,157 | 21.53% | 1,198 | 21.43% | 1,237 | 21.54% | 1,109 | 21.17% | 1,025 | 21.00% |
| 80+ | 1,241 | 23.10% | 1,290 | 23.08% | 1,393 | 24.25% | 1,289 | 24.61% | 1,168 | 23.93% |
| UNSPEC. | 35 | 0.64% | 40 | 0.72% | 74 | 1.29% | 71 | 1.35% | 25 | 0.52% |

Verispan Vector One: National, Data Extracted 2-1-06. File: VONA 1-26-07 2007-181 Oxybutynin.xls

Table 4 Projected Patients Receiving an Oxybutynin Prescription Dispensed Through Retail Pharmacies in the U.S. from 2002 through 2006, by Patient Age (years)

| | 2002 | | 2003 | | 2004 | | 2005 | | 2006 | |
|-------------------|--------------|----------------|--------------|----------------|--------------|----------------|--------------|----------------|--------------|----------------|
| | Pts (000) | Pt Share |
| Oxybutynin | 1,408 | 100.00% | 1,528 | 100.00% | 1,438 | 100.00% | 1,276 | 100.00% | 1,190 | 100.00% |
| 0 - 5 | 22 | 1.60% | 23 | 1.50% | 20 | 1.41% | 17 | 1.35% | 18 | 1.55% |
| 6 - 16 | 76 | 5.41% | 77 | 5.04% | 71 | 4.92% | 64 | 5.05% | 66 | 5.56% |
| 17 - 29 | 47 | 3.36% | 50 | 3.26% | 46 | 3.18% | 40 | 3.17% | 37 | 3.15% |
| 30 - 39 | 77 | 5.45% | 79 | 5.16% | 68 | 4.72% | 57 | 4.49% | 53 | 4.46% |
| 40 - 59 | 385 | 27.38% | 411 | 26.91% | 371 | 25.79% | 327 | 25.64% | 301 | 25.31% |
| 60 - 69 | 230 | 16.34% | 253 | 16.53% | 237 | 16.46% | 213 | 16.69% | 212 | 17.86% |
| 70 - 79 | 304 | 21.61% | 327 | 21.43% | 311 | 21.64% | 273 | 21.40% | 254 | 21.36% |
| 80+ | 291 | 20.67% | 322 | 21.09% | 318 | 22.12% | 287 | 22.52% | 265 | 22.29% |
| Unknown | 26 | 1.84% | 53 | 3.49% | 73 | 5.09% | 67 | 5.22% | 45 | 3.75% |

Verispan Total Patient Tracker, Data Extracted 1-2006 File: TPT Gish 1-30-07 2007-181 Oxybutynin.xls

Table 5 Projected Patients Receiving an Ditropan XL or Oxytrol Prescription Dispensed Through Retail Pharmacies in the U.S. from 2002 through 2006, by Patient Age (years)

| | 2002 | | 2003 | | 2004 | | 2005 | | 2006 | |
|--------------------|------------------|---------------|------------------|---------------|------------------|---------------|------------------|---------------|------------------|---------------|
| | Patient Patients | Patient Share |
| Ditropan XL | 834,739 | 100% | 887,284 | 100% | 758,978 | 100% | 616,235 | 100% | 491,388 | 100% |
| 0 - 5 | 1,617 | 0.19% | 1,784 | 0.20% | 1,215 | 0.16% | 985 | 0.16% | 715 | 0.15% |
| 6 - 16 | 23,108 | 2.77% | 26,439 | 2.98% | 24,120 | 3.18% | 21,667 | 3.52% | 19,900 | 4.05% |
| 17 - 29 | 25,941 | 3.11% | 28,231 | 3.18% | 24,708 | 3.26% | 20,142 | 3.27% | 15,841 | 3.22% |
| 30 - 39 | 45,088 | 5.40% | 46,403 | 5.23% | 36,674 | 4.83% | 27,815 | 4.51% | 20,734 | 4.22% |
| 40 - 59 | 246,034 | 29.47% | 255,522 | 28.80% | 210,977 | 27.80% | 170,221 | 27.62% | 131,812 | 26.82% |
| 60 - 69 | 144,631 | 17.33% | 153,857 | 17.34% | 130,695 | 17.22% | 108,228 | 17.56% | 91,327 | 18.59% |
| 70 - 79 | 184,943 | 22.16% | 192,418 | 21.69% | 163,820 | 21.58% | 130,443 | 21.17% | 106,617 | 21.70% |
| 80+ | 177,099 | 21.22% | 190,898 | 21.51% | 168,315 | 22.18% | 138,635 | 22.50% | 112,841 | 22.96% |
| Unknown | 15,081 | 1.81% | 30,641 | 3.45% | 39,025 | 5.14% | 33,250 | 5.40% | 16,677 | 3.39% |
| Oxytrol | | | 68,711 | 100% | 155,719 | 100% | 113,011 | 100% | 93,636 | 100% |
| 0 - 5 | | | 148 | 0.22% | 343 | 0.22% | 370 | 0.33% | 401 | 0.43% |
| 6 - 16 | | | 518 | 0.75% | 1,867 | 1.20% | 1,624 | 1.44% | 1,534 | 1.64% |
| 17 - 29 | | | 1,272 | 1.85% | 2,583 | 1.66% | 1,758 | 1.56% | 1,299 | 1.39% |
| 30 - 39 | | | 2,822 | 4.11% | 5,803 | 3.73% | 3,842 | 3.40% | 2,857 | 3.05% |
| 40 - 59 | | | 18,984 | 27.63% | 39,887 | 25.61% | 28,419 | 25.15% | 21,258 | 22.70% |
| 60 - 69 | | | 12,209 | 17.77% | 26,873 | 17.26% | 19,594 | 17.34% | 17,151 | 18.32% |
| 70 - 79 | | | 17,253 | 25.11% | 37,824 | 24.29% | 26,705 | 23.63% | 23,006 | 24.57% |
| 80+ | | | 13,886 | 20.21% | 39,024 | 25.06% | 30,258 | 26.77% | 26,579 | 28.39% |
| Unknown | | | 2,621 | 3.81% | 6,351 | 4.08% | 5,064 | 4.48% | 3,420 | 3.65% |

Verispan Total Patient Tracker, Data Extracted 1-2006 File: TPT Gish 1-30-07 2007-181 Oxybutynin.xls

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