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Subject: Bicalutamide BPCA Drug Use Review in the Pediatric Population

Drug Name(s): Casodex® (bicalutamide), bicalutamide

Application Type/Number: NDA 20-498, and others

Applicant/sponsor: AstraZeneca, and others

OSE RCM #: 2010-67

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EXECUTIVE SUMMARY

This review examines drug utilization patterns in the pediatric population (patients aged 0-16, and 17 years and older) for bicalutamide, an androgen receptor inhibitor, approved for use in the treatment of prostate cancer. Since approximately 61-63% of the bicalutamide market share was sold to U.S. outpatient retail settings from January 2007 to December 2009, this review focused on the outpatient retail pharmacy settings.

During year 2007 through 2009:

- The total number of bicalutamide dispensed prescriptions decreased by approximately 13% from around 439,000 prescriptions in year 2007 to approximately 382,000 prescriptions in year 2009.
- From January 2007 to December 2009, approximately 1,200 prescriptions were dispensed to pediatric patients, accounting for about 0.1% of the total bicalutamide dispensed prescriptions. From January 2007 through December 2009, approximately ~250 (~0.11% of total patients) unique pediatric patients received a prescription for bicalutamide in the outpatient retail pharmacy setting.
- Urology was the top prescribing specialty for bicalutamide.
- Diagnosis codes recorded for pediatric patients aged 0-16 years old were below the acceptable count allowable to provide a reliable estimate of national use, therefore no data was reported from January 2007 through December 2009 for this age group. For patients 17 years and greater, “Malignant Neoplasm of Prostate” (ICD-9 185.0) was the most common diagnosis code.

1 INTRODUCTION

Using the currently available proprietary drug use databases licensed by the Agency, this review describes outpatient drug utilization patterns for bicalutamide in the pediatric population, as well as, in the adult population for the 3 twelve-month periods from year 2007 through 2009. Bicalutamide (Casodex®) was approved on October 1995 under the trade name Casodex®, NDA 20-498.

2 METHODS AND MATERIALS

IMS Health, IMS National Sales Perspectives™ data (*see Appendix 2*) were used to determine the settings in which bicalutamide were sold. Sales of this product by number of bottles and individual packages (Eaches) sold from the manufacturer into the various retail and non-retail channels of distribution were analyzed for year 2007 to 2009 (*data not provided*).¹ During the review period, outpatient retail pharmacy settings (chain stores, independent pharmacies, food stores, and mail service) accounted for the majority of bicalutamide sales (~61-63% retail and ~26-28% mail order) with the remaining ~11-13% of the market share in non-retail pharmacy settings. Thus, the examination of bicalutamide utilization patterns focused on the outpatient setting, excluding mail order channels.

Outpatient uses were measured from SDI, Vector One®: National (VONA) from year 2007 through 2009. Patient demographics stratified by ages 0-16, and 17+ years were measured from SDI, Vector One®: National (VONA) and Total Patient Tracker (TPT) from year 2007 through year 2009 (*Appendix 2*), inclusive. Indications for use were obtained from the SDI's Physician's Drug and Diagnosis Audit (PDDA) (*Appendix 2*) for bicalutamide from year 2007 through 2009. From these data sources, estimates of the number of prescriptions dispensed, the number of unique patients who received a prescription for bicalutamide, and the number of drug mentions by office-based physicians were analyzed.

¹ IMS Health, IMS National Sales Perspectives™, Data extracted 03-2010, Source file: 1003CASO.DVR

3 RESULTS

3.1 BICALUTAMIDE MARKET AND CASODEX® UTILIZATION

Dispensed prescriptions for antineoplastic and antiandrogen products decreased by nearly 12% from approximately 500,271 prescriptions in year 2007 to 442,556 prescriptions in year 2009. Dispensed prescriptions in the pediatric population (0-16 years) accounted for ~0.1% of the total “Anti-neo Antiandrogen” market throughout the study period and decreased by 9% from 721 prescriptions in year 2007 to 655 prescriptions in year 2009. Bicalutamide and Flutamide had the majority of the market share in the pediatric population, with approximately 61% and 39%, respectively, in year 2009. (*Appendix 1: Table 1*).

During years 2007 through 2009, the projected number of bicalutamide dispensed prescriptions decreased from approximately 439,000 in year 2007 to approximately 382,000 prescriptions in year 2009, almost a 13% decrease (*Appendix 1: Table 2*).

3.2 BICALUTAMIDE AND CASODEX® UTILIZATION BY PATIENT AGE

In the pediatric population (ages 0-16 years), dispensed prescriptions for bicalutamide accounted for a cumulative total of approximately 1,200 prescriptions, about 0.1% of the total projected number of dispensed prescriptions, from January 2007 through December 2009 (*Appendix 1: Table 3*). During year 2009, approximately 400 prescriptions were dispensed to pediatric patients.

Trends for patient data were similar to that of dispensed prescription data. Pediatric patients aged 0-16 years old receiving a prescription for bicalutamide accounted for approximately 0.11% (substantially less than 1%) of the estimated total 235,000 projected unique patients (~250 patients for ages 0-16 years; and ~228,000 patients for ages 17+ years) from January 2007 through December 2009. During the most recent calendar year 2009, approximately 100 pediatric patients received a prescription for bicalutamide from outpatient retail pharmacies. Patients aged 17 years and greater accounted for approximately 90,000 patients or 94% of the product market (*Appendix 1: Table 4*).

3.3 BICALUTAMIDE UTILIZATION BY PRESCRIBING SPECIALTY

From January 2007 through December, Urology was the top prescribing specialty for bicalutamide with approximately 60% of dispensed prescriptions for the cumulative time period. Oncology was the second most common prescribing specialty with approximately 7% of dispensed prescriptions, followed by Internal Medicine with approximately 7%, and Hematology with approximately 6% of dispensed prescription over the entire review period. (*Appendix 1: Table 5*). The distribution of provider specialties prescribing bicalutamide in the outpatient retail pharmacy settings showed no substantial change during the 36-month study period (data not shown).

3.4 DIAGNOSIS ASSOCIATED WITH THE USE OF BICALUTAMIDE

According to office-based physician practices in the U.S., diagnosis codes recorded for pediatric patients aged 0-16 years old were below the acceptable count allowable to provide a reliable estimate of national use, therefore no data was reported from January 2007 through December 2009 for this age group. For patients 17 years and greater, “Malignant Neoplasm of Prostate” (ICD-9 185.0) was the most common diagnosis codes. (*Appendix 1: Table 6*).

4 LIMITATIONS

Findings from this consult should be interpreted in the context of the known limitations of the databases used. We estimated that bicalutamide 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. It does not include demographic information for the patients receiving these products, such as age and gender. 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.

Indications for use were obtained using SDI's PDDA, a monthly survey of 3,100 office based physicians. Although PDDA data are helpful to understand how drug products are prescribed by physicians, the small sample size and the relatively low usage of these products limits the ability to identify trends in the data. In general, PDDA data are best used to identify the typical uses for the products in clinical practice, and the VONA outpatient prescription data to evaluate trends over time.

SDI 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.

5 CONCLUSIONS

Dispensed prescriptions for bicalutamide in the pediatric population (ages 0-16 years) accounted for approximately 0.1% of the total projected number of dispensed prescriptions and approximately 0.1% of projected unique patients from January 2007 through December 2009. Urology was the top prescribing specialty for bicalutamide with approximately 60% of dispensed prescriptions. No diagnosis codes were reported during the 3 twelve-month periods from January 2007 through December 2009 for pediatric patients aged 0-16 years. For patients 17 years and greater, "Malignant Neoplasm of Prostate" (ICD-9 185.0) was the most common diagnosis code.

6 APPENDICES

APPENDIX 1: Tables

Table 1. Total Number of Dispensed Prescriptions by Patient Age (0-16 and 17+) for Antiandrogens in U.S. Outpatient Retail Pharmacies, January 2007 to December 2009

	2007		2008		2009		1/2007-12/2009	
	TRxs N	Share %	TRxs N	Share %	TRxs N	Share %	TRxs N	Share %
30520 ANTINEO ANTIANDROGENS	500,271	100.0%	470,620	100.0%	442,556	100.0%	1,413,447	100.0%
0-16	721	0.1%	673	0.1%	655	0.1%	2,049	0.1%
bicalutamide	411	57.0%	379	56.3%	401	61.2%	1,191	58.1%
flutamide	302	41.9%	294	43.7%	255	38.8%	851	41.5%
nilutamide	8	1.1%	--	--	--	--	8	0.4%
17+	498,803	99.7%	469,187	99.7%	441,624	99.8%	1,409,614	99.7%
bicalutamide	438,076	87.8%	410,256	87.4%	381,041	86.3%	1,229,373	87.2%
flutamide	50,451	10.1%	48,079	10.2%	49,095	11.1%	147,625	10.5%
nilutamide	10,276	2.1%	10,852	2.3%	11,488	2.6%	32,616	2.3%
UNSPEC	747	0.1%	760	0.2%	277	0.1%	1,784	0.1%
bicalutamide	685	91.7%	665	87.5%	262	94.5%	1,612	90.4%
flutamide	37	5.0%	87	11.4%	15	5.5%	139	7.8%
nilutamide	25	3.3%	8	1.1%	--	--	33	1.8%

Source: SDI, Vector One®: National. Extracted 3-3-2010. Source File: VONA 2010-67 Bicalutamide Market BPCA 3-3-10.xls

Table 2. Total Number of Dispensed Prescriptions for Bicalutamide in U.S. Outpatient Retail Pharmacies, January 2007 to December 2009

	2007		2008		2009		1/2007-12/2009	
	TRxs N	Share %	TRxs N	Share %	TRxs N	Share %	TRxs N	Share %
Bicalutamide	439,160	100.0%	411,279	100.0%	381,704	100.0%	1,232,143	100.0%

Source: SDI, Vector One®: National. Extracted 2-26-2010. Source File: VONA 2010-67 Bicalutamide BPCA 2-26-10.xls

Table 3. Total Number of Dispensed Prescriptions by Patient Age (0-16 and 17+) for Bicalutamide in U.S. Outpatient Retail Pharmacies, January 2007 to December 2009

	2007		2008		2009		1/2007-12/2009	
	TRxs N	Share %	TRxs N	Share %	TRxs N	Share %	TRxs N	Share %
Bicalutamide	439,172	100.0%	411,300	100.0%	381,704	100.0%	1,232,176	100.0%
0-16	411	0.1%	379	0.1%	401	0.1%	1,191	0.1%
17+	438,076	99.8%	410,256	99.7%	381,041	99.8%	1,229,373	99.8%
UNSPEC	685	0.2%	665	0.2%	262	0.1%	1,612	0.1%

Source: SDI, Vector One®: National. Extracted 3-1-2010. Source File: VONA 2010-67 Bicalutamide by Age BPCA 3-1-10.xls

Table 4. Total Number of Projected Patients on Bicalutamide by Patient Age in U.S. Outpatient Retail Pharmacies, January 2007 to December 2009

Patient Age (years)	2007		2008		2009		1/2007-12/2009	
	Projected Patient Count N	Total Patient Share %	Projected Patient Count N	Total Patient Share %	Projected Patient Count N	Total Patient Share %	Projected Patient Count N	Total Patient Share %
Grand Total	112,266	100.00%	106,982	100.00%	95,882	100.00%	235,147	100.00%
0 - 16	115	0.10%	105	0.10%	101	0.11%	247	0.11%
17+	110,675	98.58%	105,200	98.33%	89,805	93.66%	227,983	96.95%
UNKNOWN AGE	5,024	4.47%	5,173	4.84%	13,136	13.70%	19,123	8.13%

* 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: SDI, Total Patient Tracker, 2007-2009, Extracted February 2010. Files: TPT 2010-67 Bicalutamide (Display) BPCA 2-26-10.xls, TPT 2010-67 Bicalutamide (Aggregate) BPCA 2-26-10.xls

Table 5. Total Number of Dispensed Prescriptions for Bicalutamide in U.S. Outpatient Retail Pharmacies by Top 10 Prescribing Specialties, January 2007 to December 2009

	01/2007-12/2009	
	TRxs N	Share %
Bicalutamide	1,232,144	100.0%
UROL	742,600	60.3%
ONCOLOGY	88,665	7.2%
IM	84,304	6.8%
HEM	78,596	6.4%
GP/FM/DO	55,609	4.5%
UNSPEC	44,064	3.6%
RAD	43,854	3.6%
NP	18,291	1.5%
PA	15,697	1.3%
HOSP	15,384	1.2%
All Others	45,079	3.7%

Source: SDI, Vector One®: National. Extracted 3-1-2010. Source File: VONA 2010-67 Bicalutamide by Specialty BPCA 3-1-10.xls

Table 6. Diagnosis Associated with the Total Number of Drug Uses of Bicalutamide by Patient Age (0-16, 17+ years) As Reported by Office-Based Physician Practices, January 2007 to December 2009

	1/2007-12/2009	
	Uses (000)	Share %
Bicalutamide	954	100.0%
0-16	--	--
17+	954	100.0%
1850 MALIGN NEOPL PROSTATE	781	81.9%
1988 OTH SECONDARY MALIG NEO	80	8.4%
1991 MALIGNANT NEOPLASM NOS	37	3.9%
7909 ABN BLOOD FINDINGS NEC	26	2.7%
1985 SECONDARY MALIG NEO BONE	13	1.3%
2222 BENIGN NEOPLASM PROSTATE	4	0.4%
V670 SURGERY FOLLOW-UP	4	0.4%
5997 HEMATURIA	3	0.3%
4860 PNEUMONIA, ORGANISM NOS	3	0.3%
7185 ANKYLOSIS OF JOINT	3	0.3%

Source: SDI Physician Drug and Diagnosis Audit®: National, 2007-2009, Extracted 3-1-2010. Source File: PDDA 2010-67 Bicalutamide BPCA AgeDx4 3-1-10.xls

*Use - Projected uses for a product linked to a diagnosis. The projected number of times a product has been reported for treatment of a particular disease.

APPENDIX 2: Database Descriptions

SDI, LLC: Vector One®: National (VONA)

SDI'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 2.0 billion prescription claims per year, representing over 160 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. SDI receives all prescriptions from approximately one-third of the stores and a significant sample of prescriptions from the remaining stores.

SDI Physician Drug & Diagnosis Audit (PDDA)

SDI'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.

SDI uses the term "drug occurrences" to refer to the number of times a product has been reported on a patient information form during an office-based patient visit for that period. It is important to note that a "drug occurrence" does not necessarily result in a prescription being generated. A "drug occurrence" can result from a prescription written, a sample given, a recommendation for OTC products, recommendation with sample, a product dispensed or administered in the office, a hospital order, a nursing home order or a combination of these.

SDI, LLC: Vector One®: Total Patient Tracker (TPT)

SDI'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.

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.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22310	ORIG-1	ASTRAZENECA PHARMACEUTICA LS LP	CASODEX (BICALUTAMIDE) TABLETS

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/s/

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03/25/2010

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Drug use data cleared for background package.