M E M O R A N D U M

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

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SUBJECT: PID D030417
Drug: Isotretinoin
Topic: Isotretinoin Utilization

EXECUTIVE SUMMARY

This consult describes utilization and prescribing patterns for isotretinoin in the year prior to (1 April 2001 – 31 March 2002), and the year following (1 April 2002 – 31 March 2003), implementation of the System to Manage Accutane-Related Teratogenicity™ (SMART™), a risk management plan developed by Hoffmann-La Roche to minimize the risk of pregnancy among women taking Accutane®. Using proprietary data sources available to the Office of Drug Safety, we found similar results to the utilization data analyses reported by Hoffmann-LaRoche. We note that the number of isotretinoin prescriptions declined roughly 23% in the year following SMART compared to the previous year, suggesting that the SMART program may have influenced the number of isotretinoin prescriptions dispensed. Refill prescriptions also declined from 16.0% (n=238,000) of all isotretinoin prescriptions in the year before SMART to 2.4% (n=28,000) in the post-SMART year.

SMART appeared to have had little impact on other utilization variables such as prescribing physician specialty and patient age and gender. In the year prior to SMART, 76% of the prescriptions dispensed were written by dermatologists, similar to the proportion in the 12 months following SMART (80%). Females accounted for approximately one-half of the isotretinoin claims in both the pre- and post-SMART eras. The majority of isotretinoin claims

were from persons aged 16-29 years who accounted for 58.5% of the isotretinoin prescription claims in the year before SMART, and 59.5% of the prescriptions in the year following SMART.

METHODS

We examined IMS Health's National Prescription Audit *Plus*™ (NPA) for the total number of prescriptions (including refills) and prescriber specialty for all isotretinoin products since April 2001. NPA measures the retail dispensing of prescriptions, or the frequency with which drugs move out of retail pharmacies (including chain, independent, food store, mail order, discount houses, mass merchandiser, and long-term care pharmacies) into the hands of consumers via formal prescriptions. NPA provides national estimates of dispensed prescriptions based upon data from 22,000 U.S. pharmacies accounting for approximately 45% of all prescriptions in the U.S.

To describe the gender and age distribution of patients dispensed isotretinoin products, we examined data from AdvancePCS™, a large pharmacy benefits manager (PBM) for the time period of April 2001 through March 2003, inclusive. AdvancePCS currently manages prescription benefits for over 50 million patient lives and processing for over 300 million prescription claims annually for patients with prescription drug insurance coverage. The data are not nationally projected, and their representativeness of the U.S. population is not known.

RESULTS

In the 12-months prior to SMART (1 April 2001 – 31 March 2002), 1,508,000 prescriptions were dispensed for isotretinoin (Table 1). The number of isotretinoin prescriptions dispensed declined approximately 23% to 1,160,000 prescriptions in the first year following the implementation of the SMART program. Of the approximately 1.5 million isotretinoin prescriptions dispensed in the year before SMART, 16.0% (n=238,000) were refill prescriptions, compared to 2.4% (n=28,000) in the post-SMART year.

Generic versions of isotretinoin penetrated the market in the last quarter of calendar year 2002 (i.e., after SMART), accounting for 3.8% of the total isotretinoin prescriptions dispensed (Figure 1). Since the end of 2002, the use of generic isotretinoin products has been on the rise, with generics representing 33.2%, 46.7%, and 49.5% of the prescriptions dispensed in the first, second, and third quarters of 2003, respectively.

Dermatologists were the most common prescribers of isotretinoin, accounting for roughly three-quarters of prescriptions dispensed. The SMART program did not appear to have an effect on the distribution of isotretinoin prescribers specialities. In the year prior to SMART, 76% of the prescriptions dispensed were written by dermatologists, similar to the proportion in the 12 months following SMART (80%).

Isotretinoin use remains nearly evenly distributed between male and female patients. According to data from AdvancePCS, females accounted for 50.4% of the claims for isotretinoin in the year before SMART and 49.2% of the claims in the year post-SMART.

The age distributions for isotretinoin users were similar in the pre- and post-SMART eras (Table 2). Among female patients, isotretinoin use was most common in persons aged 16-29 years, with this age group accounting for 58.5% of the isotretinoin prescription claims in the year before SMART, and 59.5% of the prescriptions in the year following SMART.

Table 1. Utilization of Isotretinoin in the United States in the Year Preceding and Following Implementation of the SMART Program

	Pre-SMART (1 Apr 01 – 31 Mar 02)	**Post-SMART** (1 Apr 02 – 31 Mar 03)
# of Prescriptions Dispensed[a]	1,508,000	1,160,000
n (%) Refills[a]	238,000 (15.6)	28,000 (2.4)
n (%) Generic[a,b]	0 (0)	119,000 (10.3)
n (%) Prescriptions Written by Dermatologists[a]	1,073,000 (76.1)[d]	881,000 (79.9)[d]
% Female[c]	50.4%	49.2%

a US Data Source: IMS Health, IMS National Prescription Audit Plus™, for 4/01 to 3/02; accessed 03 December 2003.

b Generic version of isotretinoin became available in the last quarter of calendar year 2002

c Advance PCS™ Dimension Rx, accessed 11 December 2003

d Based upon 1,410,000 and 1,103,000 Rx's dispensed, respectively, as prescriber information was sometimes unknown or missing

Table 2. Age Distribution of Patients with Isotretinoin Claims in the United States in the Year Preceding and Following Implementation of the SMART Program*

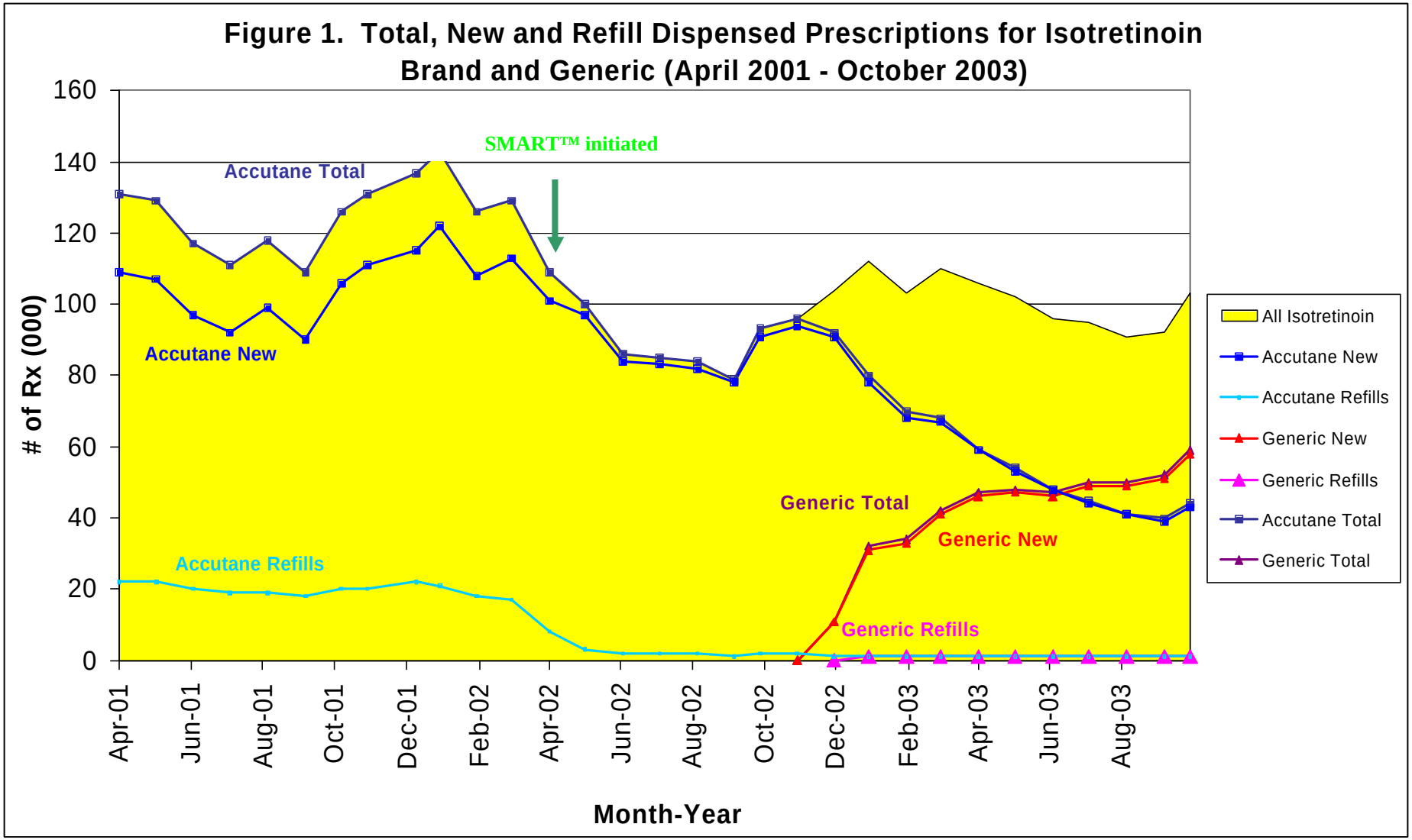
	Percent of Patients By Age Group					
	Pre-SMART (1 Apr 01 – 31 Mar 02)			**Post-SMART** (1 Apr 02 – 31 Mar 03)		
Age Group (years)	All Patients (%)	Females Only (%)	Males Only (%)	All Patients (%)	Females Only (%)	Males Only (%)
1-11	0.4	0.5	0.3	0.3	0.3	0.2
12-15	19.8	13.9	25.7	20.6	14.7	26.3
16-19	36.4	26.1	46.7	37.9	27.5	47.9
20-29	22.1	28.7	15.4	21.6	28.3	15.1
30-39	11.8	17.7	5.8	10.5	16.4	4.7
40-44	3.9	5.9	1.9	3.8	5.6	2.0
45+	5.7	7.2	4.2	5.4	7.1	3.8

* Advance PCS™ Dimension Rx, accessed 11 December 2003

CONCLUSIONS

The number of isotretinoin prescriptions declined roughly 23% in the year following SMART compared to the previous year, suggesting that the SMART program may have influenced the number of isotretinoin prescriptions dispensed. SMART appeared to have had little impact on other utilization variables such as prescribing physician specialty and patient age and gender.

Figure 1. Total, New and Refill Dispensed Prescriptions for Isotretinoin Brand and Generic (April 2001 - October 2003)



US Data Source: IMS Health, IMS National Prescription Audit Plus, for 4/01 to 10/03; accessed: 03 December 2003
Note: SMART was implemented 1 April 2002