



Published in final edited form as:

Drug Alcohol Depend. 2009 January 1; 99(1-3): 345–349. doi:10.1016/j.drugalcdep.2008.07.018.

Alcohol and Opioid Dependence Medications: Prescription Trends, Overall and by Physician Specialty

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Abstract

Over the past decade, advances in addiction neurobiology have led to the approval of new medications to treat alcohol and opioid dependence. This study examined data from the IMS National Prescription Audit (NPA) Plus™ database of retail pharmacy transactions to evaluate trends in U.S. retail sales and prescriptions of FDA-approved medications to treat substance use disorders. Data reveal that prescriptions for alcoholism medications grew from 393,000 in 2003 (\$30 million in sales) to an estimated 720,000 (\$78 million in sales) in 2007. The growth was largely driven by the introduction of acamprosate in 2005, which soon became the market leader (\$35 million in sales). Prescriptions for the two buprenorphine formulations increased from 48,000 prescriptions (\$5 million in sales) in the year of their introduction (2003) to 1.9 million prescriptions (\$327 million in sales) in 2007. While acamprosate and buprenorphine grew rapidly after market entry, overall substance abuse retail medication sales remain small relative to the size of the population that could benefit from treatment and relative to sales for other medications, such as antidepressants. The extent to which substance dependence medications will be adopted by physicians and patients, and marketed by industry, remains uncertain.

Keywords

alcoholism; opioid dependence; acamprosate; buprenorphine; disulfiram; naltrexone

1. Introduction

Few medications exist to treat substance dependence. Until 1994, only disulfiram was approved by the Food and Drug Administration (FDA) to treat alcoholism. Pharmacotherapies for opioid dependence consisted solely of methadone maintenance and naltrexone treatment. Methadone is strictly regulated federally and is not available through retail pharmacies and naltrexone has not been widely prescribed for this indication. Over the past decade, however, advances in addiction neurobiology have led to the approval of two new medications to treat alcohol dependence and one medication to treat opioid dependence (available through prescription by community physicians with appropriate federal approval). This study aimed to gain a broader understanding of the market diffusion of these medications in the United States. Although the results are not generalizable internationally,

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because the availability and use of medications to treat alcoholism and opioid dependence differs across countries, the findings may have implications for industry investment in substance abuse medications which may ultimately influence their availability in a variety of countries.

Trends in U.S. sales volume, number of prescriptions, and prices for retail medications that are FDA-approved for the treatment of alcohol dependence (i.e., disulfiram, naltrexone and acamprosate), and opioid dependence (i.e., buprenorphine) are presented. Because previous studies have shown that physician specialty is associated with early adoption of new alcoholism medications, market size potential, the receipt of ancillary psychotherapeutic services, and the level of adherence (Mark et al., 2003, Powers et al., 2002, Robinson et al., 2006), we also examined prescription volume by medical specialty of the provider.

2. Methods

This study is based on data from the IMS National Prescription Audit (NPA) Plus™ database of retail pharmacy transactions for the period of 2002 through August 2007. NPA Plus provides information on the volume of new and refilled prescriptions categorized by the specialty of the prescribing physician. The NPA Plus consists of transaction records from retail pharmacies, including those at chain, independent, food store and mass merchandiser pharmacy retail outlets. When weighted, these sources represent all prescriptions filled in retail outlets in the United States. The database does not include mail order transactions; transactions at pharmacies in HMOs serving members only; or dispensing at hospitals or clinics or directly to patients by physicians or home health agencies.

IMS collects NPA Plus information each month from a sample panel of 20,000–36,000 retail pharmacies, representing about 40% of all such pharmacies (IMS National Prescription Audit Plus™, 2005). IMS assigns physician specialty information based primarily on each physician's Drug Enforcement Administration number, which is included in a separate, larger sample of retail pharmacy transactions.

The study examined retail prescriptions of medications with FDA-approved indications for the treatment of alcohol or opioid dependence. Generic and name brand prescriptions for the following medications were examined: ReVia®/naltrexone, Vivitrol®/naltrexone IM, Antabuse®/disulfiram, Campral®/acamprosate, Subutex®/buprenorphine hydrochloride, and Suboxone®/buprenorphine hydrochloride/naloxone. For comparison purposes, data were also obtained from IMS on the number of prescriptions and sales for all antidepressants, and for one recently-marketed antidepressant, Lexapro®. Data on total dollar sales, number of prescriptions, price per prescription, and prescriptions by provider specialty were also obtained. The drivers of sales volume can be decomposed using figures for prescription volume and price. Information for the period January through August of 2007 was annualized by multiplying the data by 12/8.

3. Results

All substance dependence medications

In 2007, the number of prescriptions for alcohol and opioid dependence medications totaled 2.6 million, more than a six-fold increase from 2002 (Table 1). In 2007, nearly three times as many prescriptions were filled for opioid medications as for alcoholism medications (1,910,000 vs. 705,000, respectively). From 2003 to 2007, total dollar sales volume for retail substance dependence medications grew at a 62.2% average annual growth rate (from \$32 million to \$406 million) (Table 1). Although growth over the six-year period was strong, the market for alcoholism and opioid dependence medications remained small relative to the

antidepressant market. In 2006 more than 226 million antidepressant prescriptions were filled, equaling \$15 billion in sales.

Alcoholism treatment medications

Prescriptions for alcoholism treatment medications increased at a 12.9% average annual growth rate (from 393,000 in 2003 to an estimated 720,000 in 2007) (Table 1). The growth was largely driven by the addition of acamprosate to the alcoholism market, which occurred in 2005. Just two years after its introduction, the number of acamprosate prescriptions had grown to 293 million in 2006, surpassing those for naltrexone (Table 1). The number of prescriptions for disulfiram decreased steadily from 2003 through 2007 at an annual average rate of -3.0%. By 2007, long-acting injectable naltrexone, introduced in 2006, had captured only a small portion of the market.

As of 2007, acamprosate had the highest sales volume among alcoholism medications, reaching an estimated \$35 million, followed by oral naltrexone at \$22 million. Sales of long-acting naltrexone were only \$7 million in 2007, while sales of disulfiram were about \$14 million. To put these numbers into perspective, the antidepressant Lexapro® (escitalopram oxalate), which was first FDA approved and marketed in the United States in 2002, had a sales volume of \$987 million in 2003 and \$1.7 billion in 2004 (IMS, 2007).

The average cost per prescription varied among alcoholism medications. Long-acting naltrexone was the most expensive at \$538 in 2006, reflecting the month-long duration of action due to its sustained release formulation. Acamprosate was the next most expensive at \$108 per prescription in 2006. Naltrexone is now available as a generic medication and, on average, costs \$100 per prescription. Disulfiram is the oldest alcoholism medication on the market and has long been off-patent; in 2006, it had an average cost per prescription of \$49. However, disulfiram's cost per prescription jumped to \$78 in 2007.

As shown in Table 2, in 2006, approximately 46% of prescriptions for acamprosate and about 51% of prescriptions for naltrexone were written by psychiatrists. In contrast, only 31% of disulfiram prescriptions were written by psychiatrists. Disulfiram is more widely prescribed by general practitioners than either naltrexone or acamprosate. General practitioners wrote 29% of acamprosate prescriptions, 25% of naltrexone prescriptions, and 42% of disulfiram prescriptions. Other practitioners prescribed alcoholism medications but to a lesser extent. For example, osteopathic medicine physicians prescribed 6% of naltrexone prescriptions, 8% of acamprosate prescriptions, and 10% of disulfiram prescriptions.

Opioid addiction medications

The number of prescriptions for the two buprenorphine formulations increased from 48,000 prescriptions in the year of their introduction (2003) to 1,910,000 prescriptions in 2007. Prescriptions of buprenorphine hydrochloride (Subutex®) increased from 9,000 in 2003 to 192,000 in 2007 (Table 1). Prescriptions of buprenorphine hydrochloride/naloxone (Suboxone®) increased from 39,000 in 2003 to 1,719,000 in 2007 (Table 1).

In 2007, sales of buprenorphine formulations reached \$327 million, with buprenorphine hydrochloride/naloxone making up 87% of the total. The average prices per prescription in 2007 were \$223 for buprenorphine hydrochloride, and \$166 for buprenorphine hydrochloride/naloxone, increases of more than 100% and 50%, respectively, since their introduction in 2003.

Most prescriptions for buprenorphine hydrochloride, prescribed during the initial phase of treatment, were written by primary care practitioners (34%), followed by psychiatrists

(28%), osteopathic specialists (12%), anesthesiologists (7%), and addiction medicine specialists (4%) in 2006 (Table 2). The majority of prescriptions for buprenorphine hydrochloride/naloxone, used for maintaining abstinence from opioid use, were also written by primary care practitioners (41%), followed by psychiatrists (28%), and osteopathic physicians (12%).

4. Discussion

The IMS data represent one of the most comprehensive sources available to track retail prescription medication sales at the national level. Nevertheless, the data have limitations. Because they are prescription-level data, the number of users for each medication and their adherence to the medication regimen are unknown. IMS data do not include information on the diagnosis for which the prescriptions were written, and it is possible that some of the prescriptions included in this analysis were for non-substance dependence conditions. Moreover, other medications, not included in this analysis, are used “off-label” to treat substance use disorders.

The data indicate that sales and prescriptions for medications to treat alcoholism and opioid dependence grew rapidly following the introduction of new medications. In the alcoholism medications market, the acceptance and use of acamprosate caused overall alcoholism medication sales to approximately double from 2002 to 2007. The introduction of a long-acting formulation of naltrexone and of acamprosate may have spurred an increase in oral naltrexone prescriptions, which had previously remained relatively steady. Buprenorphine sales grew even more rapidly and exceeded those of alcoholism medications by 2007.

Despite this growth, the number of individuals receiving pharmacotherapy continues to be small relative to the large number with substance use disorders. With 7.9 million people in the United States dependent on alcohol during the period 2001-2002 (Grant et al., 2004) and only 705,000 prescriptions filled for alcoholism medications in that year, at most, approximately 9% of the population needing alcoholism treatment received the equivalent of a single prescription of a medication approved to treat the disorder. Moreover, despite a large potential market, the current sales figure for alcoholism medications may not be large enough to engender focused interest and marketing dollars from industry. No addiction medication has become a “blockbuster drug” (i.e., achieving \$1 billion in sales in any year). Because pharmaceutical companies have historically based their business model on investment in medications with the potential for a large sales volume, the sales figures for alcoholism and opioid medications may be a deterrent to additional investment in the development and marketing of new alcoholism medications (Cutler, 2007; Gilbert, 2003; Cuatrecasas, 2006).

Prior research has found a variety of obstacles to greater adoption of substance dependence medications including physicians’ perceptions of limited effectiveness, difficulty “seeing” an impact of the medication, poor information dissemination, medication adverse effects, inadequate time available to physicians for patient management, patient reluctance to take medications, and high prices of medication (Mark et al., 2003a, 2003b, 2003c, Thomas et al., 2003). Substance abuse specialty provider characteristics that have been found to be positively associated with adoption of alcoholism medications include accreditation, physician employment by the facility, integrated patient care for co-occurring psychiatric conditions, more revenue from commercial insurance, and fewer linkages with the criminal justice system (Ducharme et al., 2006). Finally, in addition to these factors, reimbursement issues may be important barriers to the greater adoption of substance dependence medications. Horgan and colleagues (2008), using a nationally representative survey, found that 31% of private insurance products excluded buprenorphine from formularies and 55%

placed it on the highest cost-sharing tier. We are unaware of research that has examined Medicaid coverage of alcoholism medications or buprenorphine but clearly the extent of Medicaid coverage would influence utilization.

Another factor that is important to consider when parsing out the drivers of adoption is the level of marketing effort exerted by the pharmaceutical company. One hypothesis as to why Campral® (acamprosate) may have diffused more rapidly than ReVia® (naltrexone) is that Forest Laboratories has been more aggressive in disseminating information about acamprosate relative to the marketing effort by DuPont Pharmaceutical Company for naltrexone. In addition, the amount of prescribing by physician specialty may also have important policy implications. Mark and colleagues found that psychiatrists adopted new antipsychotic and alcoholism medications earlier than primary care practitioners (Mark et al, 2002, Mark et al, 2003). Consistent with this evidence, our data indicate that psychiatrists appear to have adopted acamprosate earlier than general practitioners. However, we did not find that the same was true for buprenorphine hydrochloride/naloxone prescribing, perhaps because some primary care practitioners may treat addicted patients without specializing in this area. One question for future studies is whether the specialty of the prescriber influences the nature of the treatment received, such as whether patients also receive the ancillary psychosocial services that are indicated when these medications are prescribed, and their degree of adherence with these medications.

The addition of new prescription medications to treat substance dependence offers additional treatment options for patients and may encourage a different patient population to obtain treatment than that traditionally found at substance abuse treatment facilities (Johnson, 2008; Kreek et al., 2005; Kreek et al., 2002; O'Brien, 2005). Research advances may contribute to the development of new substance dependence medications with enhanced effectiveness and safety profiles (Litten et al., 2005). The level of adoption by physicians of these new medications and the degree to which the pharmaceutical industry will pursue opportunities in this area, however, remains uncertain.

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Table 1

Alcoholism and Opioid Medication Prescriptions and Sales

	2003	2004	2005	2006	2007a	Average Annual Growth Rate
Substance Abuse Medications Combined						
Prescriptions (000)	441	713	1,240	1,848	2,631	42.9%
Sales Volume (\$) (000)	\$ 36,149	\$ 72,418	\$ 149,815	\$ 251,702	\$ 405,725	62.2%
Alcoholism Medications Combined						
Prescriptions (000)	393	405	563	674	720	12.9%
Sales Volume (\$) (000)	\$ 30,801	\$ 31,706	\$ 48,698	\$ 62,383	\$ 78,093	20.5%
Individual Alcoholism Medications						
Disulfiram (Antabuse)						
Prescriptions (000)	208	212	194	182	179	-3.0%
Percent of alcoholism prescriptions	53%	52%	34%	27%	25%	
Sales Volume (\$) (000)	\$ 9,031	\$ 9,307	\$ 8,542	\$ 8,832	\$ 13,904	9.0%
Cost per prescription (\$)	\$ 43	\$ 44	\$ 44	\$ 49	\$ 78	12.4%
Naltrexone (ReVia)						
Prescriptions	185	193	184	196	221	3.6%
Percent of alcoholism prescriptions	47%	48%	33%	29%	31%	
Sales Volume (\$) (000)	\$ 21,770	\$ 22,399	\$ 20,576	\$ 20,438	\$ 22,056	0.3%
Cost per prescription (\$)	\$ 118	\$ 116	\$ 112	\$ 104	\$ 100	-3.2%
Acamprosate (Campral)						
Prescriptions (000)			185	293	306	10.6%
Percent of alcoholism prescriptions			33%	43%	43%	
Sales Volume (\$) (000)			\$ 19,580	\$ 31,499	\$ 34,802	12.2%
Cost per prescription (\$)			\$ 106	\$ 108	\$ 114	1.4%
Long-Acting Injectable Naltrexone (Vivitrol)						
Prescriptions (000)				3	15	38.0%
Percent of alcoholism prescriptions				0.4%	2.1%	
Sales Volume (\$) (000)				\$ 1,614	\$ 7,332	35.4%
Cost per prescription (\$)				\$ 538	\$ 489	-1.9%
Opioid Medications Combined						
Prescriptions (000)	48	308	677	1,174	1,911	108.9%

	2003	2004	2005	2006	2007a	Average Annual Growth Rate
Sales Volume (\$) (000)	\$ 5,348	\$ 40,712	\$ 101,117	\$ 189,319	\$ 327,632	127.7%
Individual Opioid Medications						
Buprenorphine HCl (Subutex)						
Prescriptions (000)	9	49	84	136	192	84.4%
Percent of opioid prescriptions	19%	16%	12%	12%	10%	
Sales Volume (\$)	\$ 1,005	\$ 6,483	\$ 14,373	\$ 27,324	\$ 42,780	111.7%
Cost per prescription (\$)	\$ 112	\$ 132	\$ 171	\$ 201	\$ 223	14.8%
Buprenorphine HCl/naloxone (Suboxone)						
Prescriptions (000)	39	259	593	1,038	1,719	113.2%
Percent of opioid prescriptions	81%	84%	88%	88%	90%	
Sales Volume (\$)	\$ 4,343	\$ 34,229	\$ 86,744	\$ 161,995	\$ 284,852	130.9%
Cost per prescription (\$)	\$ 111	\$ 132	\$ 146	\$ 156	\$ 166	8.3%

a. Projected based on data through August 2007

Table 2
Alcoholism and Opioid Medication Prescriptions by Physician Specialty, 2002-2006

	2002	2003	2004	2005	2006
Alcoholism					
Naltrexone					
Psychiatry	47%	54%	52%	50%	51%
Family, Internal, General	17%	24%	25%	26%	25%
Osteopathic Medicine	6%	6%	6%	6%	6%
Nurse Practitioner	2%	3%	3%	4%	5%
Other ¹	29%	13%	14%	15%	13%
Acamprosate					
Psychiatry				51%	46%
Family, Internal, General				27%	29%
Osteopathic Medicine				8%	8%
Nurse Practitioner				4%	6%
Other ²				6%	6%
Unspecified or Unknown				4%	4%
Disulfiram					
Family, Internal, General	39%	43%	43%	43%	42%
Psychiatry	26%	30%	31%	30%	31%
Osteopathic Medicine	11%	10%	10%	10%	10%
Nurse Practitioner	3%	3%	3%	4%	4%
Physician Assistant	3%	3%	3%	4%	4%
Other ³	6%	6%	5%	6%	6%
Unspecified or Unknown	12%	4%	3%	3%	3%
Naltrexone IM					
Psychiatry					100%
Opioid Addiction					
Buprenorphine HCl/naloxone (Suboxone)					
Family, Internal, General		42%	42%	42%	41%
Psychiatry		31%	29%	29%	28%

	2002	2003	2004	2005	2006
Osteopathic Medicine		11%	9%	11%	12%
Addiction Medicine		8%	6%	4%	2%
Anesthesiology		3%	2%	2%	2%
Other ⁴		-	7%	9%	11%
Unspecified or Unknown		6%	3%	3%	3%
Buprenorphine HCl (Subutex)					
Family, Internal, General		33%	36%	34%	34%
Psychiatry		33%	31%	30%	28%
Osteopathic Medicine		11%	13%	11%	12%
Anesthesiology		11%	9%	6%	7%
Addiction Medicine		11%	7%	5%	4%
Other ⁵		-	2%	11%	13%
Unspecified or Unknown		-	2%	2%	2%

- ¹ Includes neurology, pediatrics, physician assistant, addiction medicine, anesthesiology, obstetrics/gynecology, other physician specialties, and unspecified or unknown physician specialties.
- ² Includes physician assistant, addiction medicine, emergency medicine, neurology, geriatrics, anesthesiology, and other physician specialties.
- ³ Includes emergency medicine, addiction medicine, cardiology, geriatrics, and other physician specialties.
- ⁴ Includes emergency medicine, physical medicine and rehab, general surgery, obstetrics/gynecology, and other physician specialties.
- ⁵ Includes obstetrics/gynecology, neurology, general surgery, urology, emergency medicine, physical medicine and rehab, and other physician specialties.