Research on Pharmaceutical Drug Development, Use, and Outcomes

Drug Patent Expirations and the Speed of Generic Entry

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Objective. Using recent data, to analyze the generic drug entry phenomenon to determine the factors that influence the speed and likelihood of generic drug entries.
Data Sources. Data for 81 drugs that have lost patent between 1987 and 1994. Patent and exclusive marketing rights expiration dates: Food and Drug Administration's (FDA) *Approved Drug Products with Therapeutic Equivalent Evaluations* (1986–1989). Generic entry dates: *FDA Drug and Device Product Approvals* (Jan. 1987–Dec. 1994). Numbers of pending generic applications: *FDA Office of Generic Drugs Quantitative Report–ANDAs and AADAs* (Nov. 1990–Jan. 1993). Sales revenue: Pharmaceutical Data Services, Walsh-America.
Study Design. This study appropriately recognizes generic entry as a survival problem, and uses a proportional hazard method for analysis.
Principal Findings. (1) There is a negative relationship between an innovative drug's sales revenue and the time to generic entry. (2) Entries of generics tend to be slower for drugs that have either very few or a very large number of competing brands in the marketplace. (3) The time to generic entry increased overall between 1987 and 1994. (4) Drugs that primarily treat chronic symptoms tend to enter faster than the types of drugs that primarily treat acute illnesses.
Conclusions. The analysis shows that the generic industry is targeting large-revenue products and chronic drug markets. Entry of a generic drug is influenced by the existing branded substitutes in the marketplace. Surprisingly, the generic drug entry process has slowed despite many changes that would facilitate entry.

Key Words. Pharmaceuticals, generic drug entry and patent

BACKGROUND

Generic drugs are chemically identical copies of drugs that may be marketed when patents or other exclusive marketing rights on brand name drugs expire.

As many firms often make the same generic drug, generic drugs are typically sold at considerably lower prices than their original versions. Because of their price advantages and therapeutic equivalence, they are gaining wider acceptance as cost consciousness becomes increasingly important in healthcare.[1]

Once the patent and marketing exclusivity right of the innovator product expires, generic copies of such drugs may be sold with the FDA's permission. This research studies the phenomenon of generic drug entry following the expiration of patents on innovative drugs. This subject is particularly timely and important as the use of generic drugs becomes increasingly popular because of price advantages.

Generic drugs are considerably less expensive than brand name drugs. First, the cost structures of the generic firms are different from those of innovative pharmaceutical firms. The innovative pharmaceutical industry spends more than 16 percent of total revenue on research and development (Pharmaceutical Manufacturing Association 1993). In comparison, generic companies need only to invest in replicating already invented chemical molecules for manufacturing.

Second, the entry barrier to the generic industry in the form of regulatory requirements is lower than in the innovative pharmaceutical industry. The Drug Price Competition and Patent Term Restoration Act of 1984 (hereafter the 1984 Act) facilitated generic entry by requiring only a bioavailability test, but it exempts lengthy and costly clinical evaluation requirements (bioavailability tests measure the level of the drug in the human body over time without observing the effects of the drug). In fact, average expenditure on safety and clinical evaluation is 18 times larger than the cost of a bioavailability test for brand name pharmaceutical firms in the United States (Pharmaceutical Manufacturers Association 1993).

In a protected market, where firms enjoy high rates of profit, lowering or removing entry barriers entices entry. In fact, within the first year after patent expiration, an average of 17.2 generic producers enter the market for each product. The number increases to 25.1 after two years (Grabowski and Vernon 1992). Such characteristics of the generic market (e.g., relatively low entry barriers, homogeneous products, and many producers) are highly conducive to competition in this market.

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Although generic drugs have been in existence for many years, until recently they claimed only a small share of the prescription drug market. An earlier study on the effects of patent loss on 12 drugs during the 1970s found that patent loss had very little impact on the revenue of innovative drugs (Statman 1981); the brand name products, on average, were found to maintain 99 percent of their revenue, even after two years.

Recently, the generic market has been expanding. Using data from the early 1980s, Masson and Steiner (1985) found that the share of generics increased to 23.3 percent. Using the data between 1983 and 1987, Grabowski and Vernon (1992) found that, among the drugs that had generic entries in the data period, the average quantity market share of generics reached 35 percent after one year and 49 percent after two years.

Several researchers have studied the issues related to utilization of generic drugs and their effects on the innovator drugs. For example, Hurwitz and Caves (1988) studied both the market shares of innovator drugs after generic entry and the number of generic suppliers in a given market, and they found that only the sales amount variable had statistically significant explanatory power. Using data between 1983 and 1987, Grabowski and Vernon (1992) examined the number of generic suppliers in a given market to study the impact of the FDA's simplified generic approval process that resulted from the 1984 amendment. The authors found again that only the profit rate or sales revenue of the original innovator drugs was statistically significant in explaining the number of generic suppliers.

One element missing in these earlier works, however, is that they limited their scope of research solely to existing generic drugs. Contrary to popular impressions, a significant portion of off-patent drugs do not face generic entries. In fact, nearly 40 percent of off-patent drugs did not see any generic entry within two years between 1987 and 1993, and, among those that did enter, some entries had considerable delays. Given the nature of the phenomenon (i.e., high incidences of no entry and a great deal of variation in entry lag for those products that successfully enter the market), the generic entry should be understood as a continuing process, not as occurrences of discrete events.

METHODS

Because generic drug entry is recognized as a continuing process, a duration model is used for regression analysis. For timeliness, I chose the recent wave

of patent expirations: the data period spans 1987 to 1994, and it contains 77 unique chemical compounds or combinations (82 drug products) that have lost patent protection during this period[2] (See Appendix for a list of drugs).

Table 1 gives simple averages of generic entry rates and average entry lags grouped by the sales revenue of the original innovator drugs. The average figures indicate that the generic entry tends to be faster for products with larger market revenues, and that the entry rates are higher for large revenue groups. The overall rate of generic entry by January 1995 was 62.7 percent, meaning that many off-patent drugs did not face generic competition for several years. For the group with annual sales revenue of $10 million or less, less than half of the off-patent drugs faced generic competition.

Moreover, for the products that have generic competitors, the timing of entry varies greatly. Figure 1 shows the extent of delays for each revenue group. It is notable that, despite the revenue sizes, approximately half of the entries occurred almost immediately after the original innovator product lost its patent. For the remaining 50 percent of cases, however, the generic drug entry delays seemed to vary a great deal.

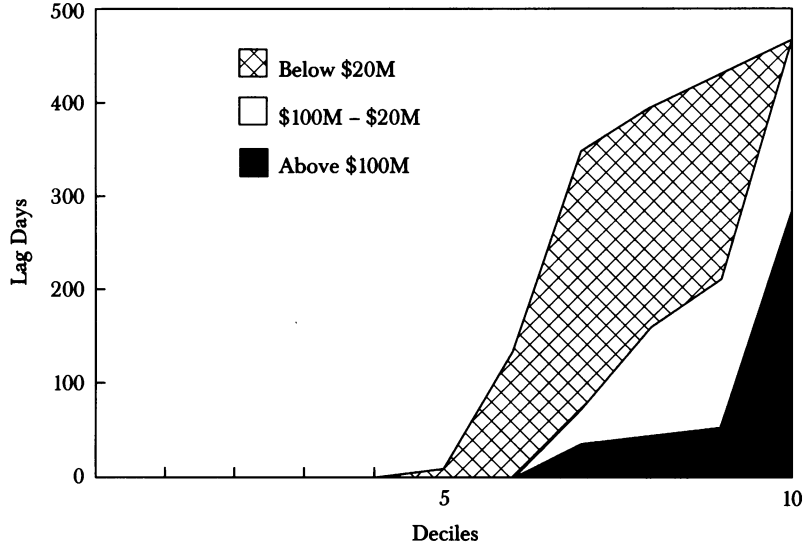
The generic entry phenomenon is a continuing process, and not merely a binary event. Additionally, since entries are possible in the future–that is, beyond the data years–we need a method that accounts for the effects

Table 1: Generic Entry Lags

Annual Sales of Brand (N = *Sample Size*)	*Average Lag Days, All Products*	*(s.d.)*	*Average Lag Days, Entrants Only*	*(s.d.)*	*% of Drugs with Generic Entry*
$100 million or higher ($N = 15$)	324.1	(652.5)	52.3	(92.1)	80
Less than $100 million but $25 million or higher ($N = 18$)	508.3	(660.9)	75.6	(136.1)	66
Less than $25 million but $10 million or higher ($N = 11$)	811.27	(930.4)	207.0	(209.7)	54
Less than $10 million ($N = 16$)	989.93	(843.8)	177.1	(178.1)	46
Total ($N = 60$)	640.44	(807.0)	85.0	(92.9)	62.7

Notes: All lags are in number of days. Standard deviations in parentheses. Sample sizes are the number of drug compounds, not the brands. The 1994 data are excluded because it seems premature to evaluate their entry status.

Figure 1: Generic Entry Delay; Entry Lag by Revenue Groups



of truncation. Thus, a type of censored duration analysis, the proportional hazard model, is used for regression. Here, the risk event is defined as an entry (birth rather than death) of the first generic version of the drug.

The generic drug firms would perceive the revenue of an innovator drug as a good indicator of profit. Thus, the decision to develop, test, and sell generic drugs will be influenced by the revenue of the brand name product.[3] To see if the time to generic entry is dependent on the prospective profitability of entry, the revenue of the brand name drug prior to patent expiration is used as a proxy variable. Alternatively, I used a class dummy variable that divides the products into three conventional groups by sales revenue: a commercially successful "blockbuster" drug group (annual revenue of $100 million or more), a moderately successful group (between $20 million and $100 million), and a not so commercially successful drug group ($20 million or below).

The generic firm's decision to enter a particular market may also be influenced by the degree of competition and perceived profitability in the market. With respect to the number of products in a market, we can posit the following relationships. Existence of a large number of other competing brand name products in a therapeutic area could mean that the industry is competitive, hence, a low level of profit. On the other hand, lack of other

brand competitors in a therapeutic area years after the introduction of the first product could signal the existence of a technological barrier to entry. Alternatively, we can hypothesize that the market demand is insufficient to support many products. Based on these hypotheses, I included variables to test such a contention. As the posited relationship is non-monotonic, the numbers of therapeutic substitutes were transformed and tested.

The pharmaceutical industry is often characterized as a highly dynamic industry. The generic industry, which competes against the brand name pharmaceutical industry, must respond to the changes in that latter industry to remain competitive. Recently, the generic drug industry has been going through a structural change. New generic companies start, while some existing firms are acquired by leading brand name pharmaceutical companies. In order to capture the possible movement toward more rapid generic entry, I include a quarterly time trend variable.

The Omnibus Budget Reconciliation Act of 1990 (OBRA 90) established the Medicaid Drug Rebate Program, which went into effect in 1991. The rebate program mandated that all generic drug manufacturers participating in the Medicaid program pay 10 percent of their total Medicaid revenue to the states. The total amount of rebates from the generic drug industry was approximately $10 million in 1993.[4] Since the rebate would reduce the profit of the industry, I include a dummy variable for the years in which the rebate program is in place.

The drugs that primarily treat chronic conditions are distinguished from the drugs that are primarily for acute conditions and time-limited therapies, as they may face different demand characteristics in the market.[5] Additionally, following the Therapeutic Category Index system in the *Physicians' Desk Reference* (Medical Economics Data Production Company 1994), all 82 drugs were grouped to see if there are systematic differences in generic entry speeds among the groups. The groupings by therapeutic indications include anti-inflammatory, anti-infective, cardiovascular, dermatological, respiratory, psychotropic, and a group inclusive of all other drugs.[6]

ESTIMATION RESULTS

Table 2 presents the estimation results from the survival regression models. The results show a negative relationship between the sales revenue of the brand name drugs under patent and the time to generic entry. Negative and highly significant coefficients of these revenue variables confirm that

commercially successful "blockbuster" drugs are more likely to face generic competition than less commercially successful drugs. Given the empirical evidence of low marginal cost-to-price ratios in pharmaceutical manufacturing, generic drug firms appear to perceive the size of brand name drug revenue as a good indicator of expected profit. Such a finding is an intuitive result; drugs that generate more revenue attract more rapid generic entries.

I conjectured that a non-monotonic relationship exists between the likelihood of generic entry and the number of other branded products within each therapeutic category. To test the hypothesized relationship, numbers of all competing brand name products within a therapeutic group were transformed and tested.[7] Among the transformations tested, taking absolute values of deviations from several points, such as mean, median, and focal numbers (e.g., 10) generally produced significant results (see Table 2, Models III–VI). Some quadratic transformations were significant (Models VII–VIII), but not jointly with the linear transformations. The positive and significant estimation results seem to support the view that generic entry is influenced by the number of competing brand name products in the market, and that the relationship is non-monotonic.

By virtue of the model, calculating the relative risk ratios by therapeutic categories is possible.[8] However, because the sample sizes in most groups are small and the variances in the lag are large, only the cardiovascular group has a statistically significant result. This would mean the expected generic entry time of cardiovascular drugs is 35 percent shorter than the comparison group of "other" products.

A certain degree of difference seems to exist between chronic and acute drugs in terms of generic entry speed. Controlling for the effects of sales revenue and period, chronic-use drugs may have faster generic entry than drugs that primarily treat acute conditions. Due to epidemiological factors, the demand for acute drugs can exhibit a higher degree of fluctuation both seasonally and across the years than does the demand for chronic drugs. Facing greater financial constraints than most innovative pharmaceutical firms, generic firms may prefer to develop products that have a more predictable demand.

The Medicare drug rebate variable has positive and significant coefficients. This indicates that, other things being equal, the generic drug entry process in the post-rebate period (1991–1994) is slower than in the pre-rebate period (1987–1990).[9] The drug rebate program evidently reduced the rate of profit in the generic industry; it is unclear, however, how much direct impact the rebate regulation had on the speed of generic entry.

Table 2: Regression Results Duration Variable, Generic Entry Delay in Days; Total Observations = 77

Variable	*Model I*	*Model II*	*Model III*	*Model IV*	*Model V*	*Model VI*	*Model VII*	*Model VIII*
Sales	−0.00438 (−2.98)***	−0.00448 (−3.09)***	−0.00521 (−3.49)***	−0.00508 (−3.413)***			−0.00486 (−3.550)***	−0.00504 (−3.466)***
Size					−0.6257 (−2.824)***	−0.6194 (−2.755)***		
Abs10		0.02557 (1.554)	0.03329 (2.282)**		0.02787 (1.646)*	0.02557 (1.554)*		
AbsMed	0.01713 (1.389)			0.03568 (2.117)**				
Quad 10							0.000657 (1.920)**	
QuadMed								0.00097 (1.948)**
Chron	−0.5463 (−1.516)*	−0.3577 (−0.903)			−0.4982 (−1.317)	−0.35774 (−0.903)		
Rebate		0.80469 (2.286)**			0.84658 (2.424)**		0.79482 (2.269)**	
Time	0.0438 (2.302)**		0.0436 (2.291)**	0.03932 (2.075)**		0.04485 (2.354)**		0.04184 (2.145)**
Log-likelihood	−143.619	−143.220	−143.684	−144.264	−143.102	−143.181	−144.314	−144.467
Chi-Sq (dof)	16.5377 (4)	17.3365 (4)	16.4079 (3)	15.2485 (3)	17.571 (4)	17.412 (4)	15.146 (3)	14.841 (3)
Significance	.00237	.001662	.000935	.001616	.00149	.001606	.001695	.001956

t-Statistics in parentheses: ***Significant at 1% level; **Significant at 5% level; *Significant at 10% level.

Note: Variable Names. Sales = Annual sales revenue; Size = 3 groups by sales revenue; Abs = Deviations in absolute number from*; Quad = Quadratic transformation of Abs*; Chron = Drugs mainly used for chronic illness; Rebate = Dummy for Medicaid rebate period; and Time = Quarterly time trend variable.

The quarterly time trend variable has positive coefficients with significance. This implies that, controlling for several factors, the underlying speed of generic entry has declined over the years. Using 1983–1987 data, Grabowski and Vernon (1992) analyzed the markets for 18 large drugs and concluded that the 1984 Act stimulated generic drug competition. This study, however, finds that generic competition, as measured by the rate and speed of new generic entries, has slowed in the subsequent period between 1987 and 1994.

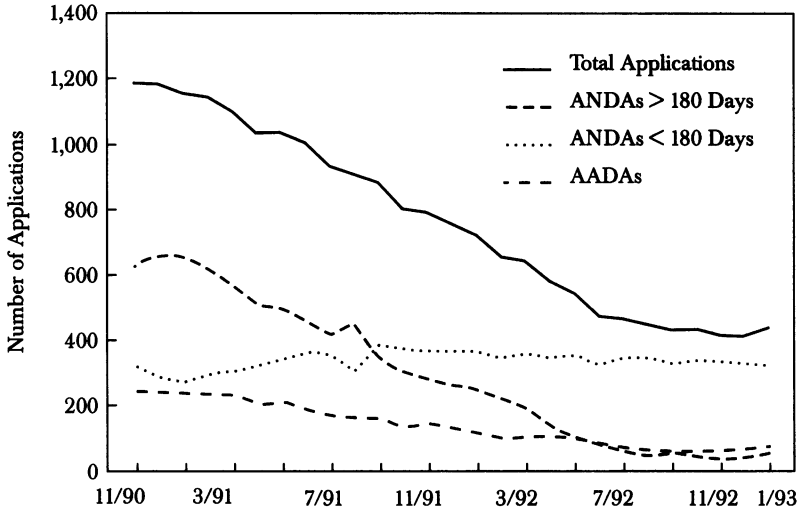
To see if the FDA is responsible for slower generic entry, I examined the numbers of generic applications awaiting review from the data period. The monthly figures of "new" generic drug applications awaiting review were obtained from two types of drug application categories, the Original Abbreviated New Drug Applications (ANDA) and the Abbreviated Antibiotic Drug Applications (AADA), from the Office of Generic Drugs, Food and Drug Administration. Figure 2 shows the total number of ANDAs and AADAs awaiting the FDA's approval decision by month. The total number of applications waiting for action has declined from more than 1,200 in October 1990 to about half that by the end of 1992. Moreover, the number of applications waiting for more than six months has dropped from more than 600 in late 1990 to just about 40 by 1993. Compared with this trend, the numbers of ANDAs pending review for less than six months have not changed much. The evidence from the FDA review process suggests that the FDA's approval process was not a factor in slowing the entry of generic drugs.

This period in the generic drug industry can be characterized as a time of structural changes. Activities on the supply side of the generic market include the entrance of new firms as well as consolidations through acquisitions and mergers. Notable activities on the demand side include rapid growth of the managed care sector as significant buyers and the increasing popularity of mail order pharmacies. Because of many confounding factors that affected the generic drug industry, it is difficult to determine what the primary factors were and to what extent each factor was responsible for the slowing down.

CONCLUSIONS

Recognizing the generic drug entry process as a duration problem, this article examined the factors that affect generic entry speed and likelihood in a truncated survival analysis framework. The data include 81 drugs that lost patent between 1987 and 1994. This period contains by far the largest wave

Figure 2: FDA Generic Review Status; Number of Pending Applications



of patent expirations of brand name drugs in terms of the number of expired patents and their total revenue.

Several findings resulted from this study. The analysis shows that the generic industry is targeting large-revenue products. Such a finding is an intuitive result that confirms earlier research findings: drugs that generate more revenue attract more rapid generic entries. Generic entry rates are found to be related to the number of existing name brand products in the same therapeutic market. Entries of generics tend to be slower for the drugs that have either very few or very many competing brands in the marketplace. The regression analyses find that product development in the generic drug market has slowed despite many changes conducive to faster entry. As this data period was a time of great volatility for the generic drug industry, it is difficult to determine what the primary factors were and to what extent they were responsible for the slowing down. Finally, drugs that primarily treat chronic symptoms tend to enter faster than the types of drugs that primarily treat acute illnesses. Greater stability of demand seems to be a factor that attracts generic entry more to the chronic drugs than to the acute drugs.

In this increasingly cost-conscious healthcare era, generic prescription drugs are gaining greater acceptance as lower-cost alternatives to brand name drugs. Because patents on many more brand name products are expiring in the pharmaceutical market, the significance of the generic drug market is

bound to increase in the future. Both the long-term and short-term implications of the recent structural changes in the generic drug industry are important research topics for the future. More research is necessary to update and further our understanding of this dynamic and evolving industry.

APPENDIX

List of Drugs with Expired Patent/Exclusivity

Brand Name	*Chemical (Generic) Name*	*Therapeutic Group*	*Patent Expiration*	*Generically Available*†
Accutane	isotretinoin	Dermatological	05/92	N
Adriamycin	doxorubicin	Anti-infective	06/88	Y
Amikin	amikacin	Anti-infective	12/90	N
Ancef	cefazolin	Anti-infective	06/87	Y
Annaprox	naproxen sodium	Anti-inflammatory	12/93	Y
Ascendin	amoxapine	Psychotropic	08/89	Y
Bactrim	sulfamethazola/ trimethoprim	Anti-infective	06/87	Y
Beclovent	beclomethasone	Respiratory	08/94	N
Blocadren	timolol	Cardiovascular	04/89	Y
Brethine	terbutaline sulfate	Respiratory	03/94	N
Bumex	butametanide	Cardiovascular	02/93	N
Bricanyl	terbutaline sulfate	Respiratory	03/94	N
Cardizem	diltiazem	Cardiovascular	11/92	Y
Ceclor	cefaclor	Anti-infective	12/92	N
Cleocin	clindamycin	Anti-infective	02/87	Y
Clinoril	sulindac	Anti-inflammatory	04/89	Y
Colestid	colestipol	Cardiovascular	09/89	N
Corgard	nadolol	Cardiovascular	09/93	Y
Corzide	nadolol	Cardiovascular	09/93	Y
Depo-Provera	medroxyprogesteron	Contraceptive*	07/94	N
Diabeta	glyburide	Diabetes Agent*	05/94	Y
Dobutrex	dobutamine	Cardiovascular	10/93	Y
Dolobid	diflunisal	Anti-inflammatory	04/92	Y
Duricef	cefadroxil	Anti-infective	03/89	Y
Feldene	piroxicam	Anti-inflammatory	04/92	Y
Flexeril	cyclobenzaprine	Muscle Relaxant*	05/92	N
Forane	isoflurane	Anesthetic*	01/93	Y
Glucotrol	glipizide	Diabetes Agent*	05/94	N
Halcion	triazolam	Psychotropic	10/93	Y
Heptavax	heptavax	Hepatitis Vaccine*	06/89	N
Intal	cromyln sodium	Respiratory	08/89	Y
Keflex	cephalexin	Anti-infective	04/87	Y
Kefzol	cefazolin	Anti-infective	06/87	Y
Lopid	gemfribizil	Cardiovascular	07/89	Y
Lopressor	metoprolol tartrate	Cardiovascular	12/93	Y
Loxitane	loxapine	Psychotropic	12/87	N

continued

Brand Name	*Chemical (Generic) Name*	*Therapeutic Group*	*Patent Expiration*	*Generically Available†*
Lozol	indapamide	Cardiovascular	07/93	N
Lidex	fluocinonide	Dermatological	07/88	Y
Mandol	cefamandole	Anti-infective	02/89	N
Micronase	glyburide	Diabetes Agent*	05/94	Y
Minipress	prazosin	Cardiovascular	05/89	Y
Moduretic	amiloride	Cardiovascular	12/90	N
Mucomyst	acetylcysteine	Respiratory	01/88	Y
Nalfon	fenoprofen	Anti-inflammatory	08/87	Y
Naprosyn	naproxen	Anti-inflammatory	12/93	Y
Nasalcrom	cromyln sodium	Respiratory	08/89	Y
Nebcin	tobramycin	Anti-infective	09/89	N
Nicorette	nicotine polacrylex	Nicotine Gum*	01/94	N
Norcuron	vercuronium bromide	Muscle Relaxant*	04/94	N
Nordette	ethynyl estradiol	Contraceptive*	11/91	Y
Normodyne	labetarol HCL	Cardiovascular	08/94	N
Omnipen	ampicillin	Anti-infective	01/87	Y
Ovral	ethynyl estradiol	Contraceptive*	11/91	Y
Parlodel	bromcriptine	Parkinsonism*	08/90	N
Pamelor	nortriptyline	Psychotropic	11/92	Y
Pepsid	famotidine	H-2 Blocker*	10/91	N
Procardia	nifedipine	Cardiovascular	01/91	Y
Propine	dipivefrin HCL	Ocular*	06/91	N
Proventil	albuterol	Respiratory	02/89	Y
Retin-A	tretinoin	Dermatological	04/90	N
Ridaura	auranofin	Anti-inflammatory	01/92	N
Seldene	terfenadine	Anti-histamine*	04/92	N
Ser-Ap-Ez	reserpine hydraxine	Cardiovascular	06/87	N
Sinemet	carbiodopa/levodopa	Parkinsonism*	08/91	Y
Spectrobid	bacampacillin	Anti-infective	03/92	N
Tagamet	cimetidine	H-2 Blocker*	05/94	Y
Tenoretic	atenolol	Cardiovascular	09/91	Y
Tenormin	atenolol	Cardiovascular	09/91	Y
Tolectin	tolmetin sodium	Anti-inflammatory	08/90	Y
Trandate	labetalol HCL	Cardiovascular	08/94	N
Tranxene	clorazepate	Psychotropic	05/87	Y
Trental	pentoxifylline	Cardiovascular	08/94	N
Triphasil	ethynyl estradiol	Contraceptive*	11/91	Y
Vanceril	beclomethasone	Respiratory	08/94	N
Ventolin	albuterol	Respiratory	02/89	N
Vepesid	etoposide	Antineoplastic*	11/93	N
Visken	pindolol	Cardiovascular	09/92	Y
Xanax	alprazolam	Psychotropic	10/93	Y
Zinacef	cefuroximine	Anti-infective	08/94	N
Zyloprim	alluprinol	Gout	11/88	Y

*Grouped as "others" in regression.

**Generic availability as of January 1995.

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NOTES

1. One of the factors that contributes to a greater use of generic drugs is the increasing prevalence of generic substitution in the managed care sector. In addition, recent growth of the managed care sector may have helped to increase the demand for generic drugs. Nearly all HMOs adopted a generic substitution policy (97.9 percent), and the generic drug use rate has grown from 36 percent in 1993 to 45 percent in 1995 (Ciba-Geigy Corporation 1994, 1995).
2. The information on expiration of patents and marketing exclusivity was from the Food and Drug Administration's (FDA) *Approved Drug Products with Therapeutic Equivalent Evaluations*. The information on generic entry was collected from the *FDA Drug and Device Product Approvals* as the first approval date of a generic drug of a kind. The differences in the dosage levels and methods of delivery (e.g., pills, injectables, topicals, or inhalants) were ignored. The sales revenue data are from the Pharmaceutical Data Services, Walsh-America.
3. Constructing profit rates of brand name drugs can be done using the prices of generic drugs as proxies for marginal costs. However, as this study deals with a significant number of non-entry cases as well, this method cannot be used. Production costs are estimated to be, on average, less than 30 percent of the revenue for a sample of large U.S.-based companies (Comanor and Schweitzer 1994). Grabowski and Vernon (1992) used both the estimated profit rate and sales revenue variables in their study on entry cases; they found little difference in the result as the two variables are highly correlated.
4. The rebate rate for the generic drugs began as 10 percent of average manufacturer's price (AMP) in 1991, and subsequently increased two years later to 11 percent of AMP. The rebate rate for branded drugs is currently at 15.1 percent of AMP.
5. It appears that there is no generally accepted standard chronic/acute drug classification system. For this study, the drugs in the data are classified into three groups: primarily chronic therapy, primarily acute therapy, and time-limited therapy. Most drug classifications are straightforward in following therapeutic groupings (e.g., vaccines and most anti-infectives for acute use, and asthma and Parkinsonism drugs for chronic use). However, if a time limit is recommended for a drug regimen, the drug is classified in the third group. Some drugs that are for both long-term use and short-term use (e.g., oral contraceptives and allergy medications) are classified in the third category. Kathleen Gondek, Ph.D., R.Ph. helped to design the categories and identify drugs for each group.
6. The therapeutic groupings followed the Product Category Index used in the *Physicians' Desk Reference* (1994). Anti-inflammatory drugs include both steroidal and nonsteroidal anti-inflammatory agents and gold compounds. Anti-infective

drugs include various antibiotic drugs and sulfa drugs. Cardiovascular drugs include ACE-inhibitors, beta-blockers, calcium channel blockers, antilipemics, and diuretics. Dermatological preparations include a variety of drugs such as acne medications, corticosteroids, and antifungal agents. Psychotropic drugs include benzodiazepines and antidepressants. Respiratory drugs include various bronchodilators and asthma medications. The "other drug" categories include all drugs that do not fit into the aforementioned categories. They consist of oral contraceptives, hepatitis vaccines, H-2 blockers, muscle relaxants, antihistamines, blood glucose control drugs, transdermal nicotine patches or nicotine polacrylex gum, amenorrhea/fertility drugs, antineoplastic drugs, diarrhea medications, and ocular drugs.

7. The number of other branded products variable was constructed from the total number of other brand name products in each therapeutic group found in the Product Category Index pages of the *Physicians' Desk Reference* (1994).
8. The relative risk ratios and percentage differences in entry delay are estimated by therapeutic categories and reported as follows:

	Relative Risk Coefficient	*% Difference*	*Significance*
Anti-inflammatory	−0.355	−29.88	NS
Anti-infective	0.360	43.33	NS
Respiratory	0.468	59.67	NS
Cardiovascular	−0.438	−35.46	10%
Dermatological	0.656	92.70	NS
Psychotropic	−0.348	−29.39	NS
Others	0	0	*

9. The Chow test result indicates a structural break between pre- and post-rebate years. When the model specification includes both the Medicaid rebate variable and the trend variable, the rebate variable becomes insignificant.

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