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DOCKET ALARM

Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market

By Ernst R. Berndt, Linda Bui, David R. Reiley, and Glen L. Urban*

Introduced into the United States in 1977, Tagamet was the pioneer product in the class of antiulcer drugs known as H_2-antagonists. By promoting ulcer healing through inhibiting acid secretion, Tagamet was able to heal ulcers and treat pre-ulcer conditions pharmacologically on an outpatient basis, thereby substituting for more costly hospital admissions and surgeries. In 1983 another H_2-antagonist called Zantac entered, and by early 1987 U.S. Zantac sales surpassed those of the pioneering Tagamet. Today there are four H_2-antagonists sold in the United States: Tagamet, Zantac, Pepcid, and Axid. Zantac is now the world's largest selling prescription drug, having estimated worldwide sales in 1994 of about $4 billion. Each of the four H_2-antagonists is among the top 100 in world drug sales, although Tagamet lost U.S. patent protection on May 17, 1994.

In this paper we examine empirically the role of information in facilitating and explaining growth of the overall antiulcer drug market, as well as in shaping the changing market shares of the four patented products. The dissemination of information is due largely to the use of marketing channels, such as visits by manufacturers' representatives to physicians (called "detailing"), advertising in medical journals, and most recently, by direct-to-consumer advertising. We examine these and also explore pricing policies, product differentiation, and order-of-entry effects.

I. Background

There are two cost conditions that have considerable bearing on the structure and behavior of the pharmaceutical industry. First, sunk costs are very large. In particular, the costs of bringing a product to market (doing basic research, winning patent approval, engaging in development, performing clinical trials, and obtaining final approval from the Food and Drug Administration [FDA]) are currently estimated at about $360 million per drug. Second, for most traditional pharmaceutical products, the marginal costs of manufacturing are very small. Although appropriate cost data are not publicly available, it is not uncommon for generic drugs to sell at 25–30 percent of the pre-patent-expiration price. Informal discussions with industry officials suggest that for the H_2-antagonists, production costs are about 10–25 percent of the price.

These cost conditions have implications for pricing. Patent protection gives firms the ability to influence price, and to the extent one is willing to use the Lerner markup relation as a pricing rule of thumb, one would expect price and marginal-cost conditions to approximate $(P - \mathrm{MC})/P = -1/\varepsilon_p$, where ε_p is the demand price elasticity. With manufacturing costs at 10–25 percent of price (markups 75–90 percent), the implied demand price elasticity would range from -1.1 to -1.3. However, elasticities of that size contrast with the common perception that demand for prescription drugs is extremely price inelastic. Peter Temin (1980 Ch. 5), for example, notes that physicians traditionally have been relatively unaware of drug prices. Other observers have suggested that moral hazard in the form of third-party (insurance) payment practices also contributes to low price responsiveness. Very little econometric evidence on demand elasticities for drugs is available, in part because the traditional consumer demand paradigm (utility maximization, marginal rates of substitution equal to relative marginal prices, etc.) cannot be expected to describe behavior adequately in a market in which principal–agent problems (stemming from relationships among physicians, patients, and insurers) are widespread.[1] In this paper we report elasticity estimates viewed from the vantage of the firm, not the "consumer"—whoever that may be.

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Since marginal production costs are small, enhancing revenues is essentially the same as increasing profits, and thus drug firms face strong incentives to shift out the demand curves. Thus it is not surprising that marketing–sales ratios are quite high in the pharmaceutical industry. The largest component (70–80 percent) of marketing has traditionally involved detailing to physicians; it consists of a company representative providing as much product information as possible to physicians, given the typical short time of the visit (3–10 minutes) and the content regulation enforced by the FDA. Medical journal advertising is also carried out but is less extensive than detailing. Finally, in the last few years, pharmaceutical companies have increasingly employed direct-to-consumer advertising in various media.

The information content of marketing efforts deals primarily with product differentiation and nonprice aspects. In the H_2-antagonists market, five quality attributes are of particular importance.[2] First, the various H_2-antagonists are viewed as being roughly similar in efficacy (the four- to six-week treatment healing rate is about 70–80 percent for duodenal ulcer patients), although there is some evidence suggesting that Zantac has a significantly lower relapse rate than does Tagamet for patients on duodenal maintenance treated at recommended dosages (see K. R. Gough et al., 1984). Second, less frequent dosages are thought to enhance patient compliance. When Zantac entered the U.S. market in 1983, its twice-daily dosing frequency was considered more favorable than the regimen of four times a day recommended for Tagamet. Tagamet responded with a twice-a-day version in late 1984, after which considerable rivalry ensued; today all four H_2-antagonists have a once-a-day version. A third quality attribute involves adverse interactions with other drugs. Here Tagamet has been on the defensive, for early on it was discovered that Tagamet interacted with the liver and kidney system in a way that could affect the metabolism of other drugs. As of 1994, Tagamet had reported to the FDA significant drug interactions with ten other drugs, whereas Zantac and Axid had only one reported drug interaction, and Pepcid had none. A fourth quality characteristic involves side effects. Here again Tagamet has been somewhat on the defensive, for conditions such as mental confusion in the elderly and gynecomastia (breast swelling) for males are apparently not as prevalent with Zantac, Pepcid, and Axid. Finally, the four products compete in terms of medical conditions (indications) for which the FDA has granted treatment approval. Although Tagamet was the first to win approval for the treatment of duodenal ulcers, duodenal ulcer maintenance, and gastric ulcers, in 1986 Zantac was the first to obtain approval for gastroesophageal reflux disease (GERD), a rather common condition that ranges from modest heartburn and acid indigestion to being a very serious condition. The FDA permits marketing only for approved indications. Although Tagamet obtained FDA approval for GERD in 1991, and even though Tagamet had very similar effects to Zantac, suggesting that it would likely also be effective in treating GERD, not having FDA approval for GERD

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[1] See, however, Michael Baye et al. (1994).

[2] For more extensive discussion, see Berndt et al. (1994).

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(whereas Zantac did) may have constituted a significant marketplace disadvantage for Tagamet.

In terms of pricing, at entry Zantac was priced at an 80-percent premium over Tagamet, but by May 1994 this premium had gradually declined to 19 percent. In May 1994, the price per day's treatment (to drug stores) was \$2.61 for Zantac, \$2.56 for Axid, \$2.30 for Tagamet, and \$2.17 for Pepcid; quantity shares for the four products were 49 percent, 12 percent, 22 percent, and 17 percent, respectively.

To understand the roles of marketing, pricing, and quality attributes in explaining the growth and changing composition of the H_2-antagonist market, we now outline an econometric model first for the H_2-antagonist industry as a whole, and then for the market shares garnered by the four H_2-antagonist drugs.

II. An Econometric Model of the H_2-Antagonist Market

At the industry level, we expect the quantity demanded (number of patient days of duodenal-ulcer therapy) to depend on price per treatment day, various marketing efforts, and quality attributes. Since marketing efforts provide long-lived information, it is important that cumulative information stocks be distinguished from current-period new information flows. Define the cumulative marketing information stock S_t at end of month t as

$$(1) \qquad S_t = (1-\delta)S_{t-1} + F_t = \sum_{\tau=0}^{t} (1-\delta)^{\tau} F_{t-\tau}$$

where F_t is the flow of new marketing information efforts during month t, and δ is the monthly depreciation rate. Since δ is unknown, we estimate it econometrically. In terms of marketing efforts, we distinguish three channels: the minutes of detailing to physicians (DET), the number of pages of medical-journal advertising (PJL), and the target rating points of direct-to-consumer advertising (DCA).[3] It is worth noting that the DCA efforts for H_2-antagonists did not mention any drug by name, but only encouraged viewers to seek advice from their physician if they experience heartburn and acid indigestion.

Although such DCA advertising is plausibly intended to augment overall industry demand, when two or more products exist, marketing efforts are often only focused on a particular brand. During its monopoly era, Tagamet recouped all the benefits of its marketing efforts (it had 100 percent market share).[4] However, once Zantac entered, even though rivalry between Tagamet and Zantac was intense, some of Tagamet's marketing efforts might have spilled over to the benefit of Zantac, and vice versa. Similarly, once Pepcid and Axid entered, while marketing efforts were typically focused on specific brands, spillovers to Zantac and Tagamet might have occurred. To allow for marketing spillovers affecting industry (rather than just product-specific) demand, we define the effective industry marketing stock S_t^* as a weighted sum of the marketing information stocks originally formed in various market structures:

$$(2) \qquad S_t^* = \mu_1 S_{1t} + \mu_2 S_{2t} + \mu_3 S_{3t} + \mu_4 S_{4t}$$

where S_{1t} is the surviving marketing information stock at end of month t that originally accumulated in the Tagamet monopoly era, S_{2t} is the similar stock formed during the Tagamet-Zantac duopoly, S_{3t} is that from the Tagamet-Zantac-Pepcid triopoly, and S_{4t} is that from the Tagamet-Zantac-Pepcid-Axid rivalry. Since in a monopoly *all* marketing efforts affect industry demand, we normalize the μ's by setting $\mu_1 = 1$.

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[3] Target rating points are defined as the target reach (the percentage of the over-age-35 population who view the message over the course of the ad campaign) times the frequency, where frequency is the number of times the average target individual views the message. For further discussion, see Philip Kotler (1991 pp. 606–8). The proprietary DCA data were kindly provided us by Lowe & Partners/SMS in cooperation with Glaxo, Inc.

[4] The discussion that follows is based in large part on Berndt et al. (1994).

Several interesting hypotheses involve the μ's. First, if the effectiveness of firms' marketing on *industry* sales is independent of market structure, then $\mu_2 = \mu_3 = \mu_4 = 1$. Second, if in the presence of competition marketing efforts only affect market shares and have a zero-sum impact on industry demand, then $\mu_2 = \mu_3 = \mu_4 = 0$. Finally, if the industry sales-augmenting effects of firms' marketing decline as the number of products in the industry increases, then $1 > \mu_2 > \mu_3 > \mu_4 > 0$.

For our industry demand equation, we specify a log-log model, where Q_t is quantity, P_t is CPI-deflated price, DET_t^*, PJL_t^*, and DCA_t^* are the effective industry stocks defined in (1) and (2), and DGERD is a dummy variable taking on the value of 1 following FDA approval for GERD:

$$\text{LNQ}_t = \beta_0 + \beta_1 \text{LNP}_t + \beta_2 \text{LNDET}_t^* + \beta_3 \text{LNPJL}_t^* + \beta_4 \text{LNDCA}_t^* + \beta_5 \text{DGERD}_t + \varepsilon_t. \tag{3}$$

Since the effective industry marketing stocks depend nonlinearly on the μ's and δ's, and since marketing efforts, pricing, and quantity demanded are likely to be jointly determined (see Richard Schmalensee 1972), we estimate parameters in equation (3) by nonlinear two-stage least squares (NL-2SLS).[5]

Our econometric model of market shares follows Urban et al. (1986) in specifying variables relative to the incumbent (Tagamet). In particular, using a log-log framework, we specify that in month t, demand quantities of product j relative to the incumbent [$\ln(Q_j/Q_1) \equiv \text{LNQJ1}$, $j =$ Zantac, Pepcid, Axid] depend on: relative prices, LNPRJ1; relative detailing and journal-pages marketing stocks, LNDTJ1 and LNJPJ1; the number of adverse drug interactions for product j relative to Tagamet, LNINTJ1;[6] a discrete variable, DSGERD, indicating whether product j has a GERD indication advantage relative to Tagamet (1, advantage; 0, no advantage; -1, disadvantage); an order-of-entry variable, ENTRY, taking on the value of 2 for all Zantac observations, 3 for Pepcid, and 4 for Axid; and an AGE variable indicating the number of months product j has been in the marketplace. Again, an instrumental-variable procedure is employed to allow for simultaneity.

Our data sources are described more fully in Berndt et al. (1994).[7] The direct-to-consumer marketing data are for a campaign begun by Glaxo (the manufacturer of Zantac) in June 1992, and they extend through May 1994.

III. Econometric Results

Based on 201 monthly observations from September 1977 through May 1994, we estimated parameters of equation (3) for the industry using NL-2SLS. To be parsimonious in parameters, we constrained the μ's and δ's to be the same for the DET and PJL marketing stocks, but allowed δ to differ for DCA. The preferred model was chosen based on the lowest value of the traditional NL-2SLS residual criterion function.

Our estimated H_2-antagonist *industry* price elasticity is -0.689 ($t = 3.80$), while elasticity estimates for the DET, PJL, and DCA surviving stocks are 0.553 ($t = 7.52$), 0.198 ($t = 2.79$) and 0.008 ($t = 2.67$).[8] Hence, industry demand is positively affected by all three of the firms' marketing channels, but DET is most effective; the sum of the three marketing elasticities is 0.759, suggesting decreasing returns to scale. In terms of

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[5] As instruments, we employ the producer price index for intermediate goods, production worker wages in the pharmaceutical industry, cumulative marketing efforts by the four companies on non-H_2-antagonist products for each of the three instruments, and time.

[6] To accommodate zeros, 1.0 is added to both the DCA and the INT variables.

[7] Here we extend the Berndt et al. (1994) data base to May 1994. Data on prices, quantities, detailing, and journal pages are from IMS International.

[8] The equation R^2 is 0.995, and the Durbin-Watson statistic is 1.912.

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