The Impact of Off-Patent Drug Acquisitions on Prices

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From 2010 to 2015, more than 300 off-patent drugs sold in the USA experienced price increases of 100% or more,¹ including, for example, Turing Pharmaceutical's 5500% increase in the price of pyrimethamine. Insufficient competition may be partly to blame,² as pharmaceutical companies can acquire these drugs and dramatically raise their prices, even though patent protections or other market exclusivities have expired.^{3, 4}

OBJECTIVE

The aim of this study is to examine prices of off-patent drugs originally approved by the Food and Drug Administration (FDA), which exist in monopolies or duopolies,⁵ and were acquired by a new company after 2000.

METHODS

We identified all brand-name drugs in tablet or capsule formulation approved by FDA since 1939. We focused on drugs in tablet or capsule formulation since inhaled drugs and many injectable drugs often use medical device technology subject to its own market exclusivity considerations, whereas infused drugs are predominantly purchased by hospitals and physician facilities. We excluded over-the-counter drugs, biologic therapies, non-marketed drugs, reformulated drugs, and drugs with current patent protections or other market exclusivities. We then limited our sample to those brand-name drugs with 0 or 1 FDA-approved bioequivalent generic versions, as of April 2017. We specifically focused on monopolies and duopolies because the lack of

competition makes products more susceptible to price increases.²

For each brand-name drug, we determined whether its manufacturer had undergone a merger or acquisition or had transferred the drug license to another manufacturer (hereafter “drug acquisitions” or “acquired drugs”), using a Bloomberg Terminal, company press releases, Security and Exchange Commission filings, and news sources. Next, we collected all available wholesale acquisition costs for each brand-name drug and, if one was available, its generic version, using a Bloomberg Terminal. Depending on whether drug prices were available (Fig. 1), we used Wilcoxon matched-pairs signed-rank tests to compare prices before and after the most recent, post-2000 brand-name drug acquisition, as well as to compare the median brand-name and generic prices of both acquired and non-acquired drugs, using the most recent price available. Statistical analyses were performed using Stata 12.0 (StatCorp; College Station, TX) using a *p* value of 0.05.

RESULTS

Among 67 FDA-approved brand-name drugs with 0 or 1 currently marketed generics, 37 (55%) were acquired at least once since 2000, whereas 30 (45%) had not been acquired (Table 1). Among acquired brand-name drugs with pre- and post-acquisition prices (*n* = 37), the median post-acquisition price was significantly higher than the median pre-acquisition price (\$11.05 [interquartile range (IQR), \$3.99–\$25.82] vs. \$4.69 [IQR, \$1.97–\$14.83]; *p* < 0.001). Using the most recently available prices, the median price of acquired brand-name drugs (*n* = 37) was higher, though not statistically significant, than that of non-acquired drugs (*n* = 26) (\$22.12 [IQR, \$5.20–\$95.51] vs. \$8.60 [IQR, \$3.14–\$41.27]; *p* = 0.06). Finally, of the 67 brand-name drugs, 23 (34%) had 1 generic version. Using the most recently available prices, the median price of generic versions of acquired brand-name drugs (*n* = 10) was higher, though not statistically significant, than the median price of generic versions of non-acquired brand-name drugs (*n* = 12) (\$9.26 [IQR, \$2.23–\$97.87] vs. \$3.70 [\$1.44–\$20.08]; *p* = 0.36).

Fig. 1 Sample of FDA-approved off-patent drugs in monopolistic or duopolistic markets.

DISCUSSION

Among FDA-approved, off-patent brand-name drugs in tablet or capsule formulation and in monopolies or duopolies, more than half were acquired since 2000, with their median price more than doubling after acquisition. These findings suggest that Turing's acquisition of pyrimethamine was not an isolated event and companies may be targeting these drugs for acquisitions and subsequent price increases. Acquired drugs were priced more expensively than non-acquired drugs, though the

differences were likely not statistically significant because of the relatively small number of drugs in monopolies or duopolies, which also limits the generalizability of our findings, as well as the inconsistent availability of pricing information.

Individual companies have drawn public ire for raising drug prices after acquisition, and in most cases, acquisitions do not lead to drug or delivery modifications, providing no additional value for patients or justification for price increases. Theoretically, the solution would be to cap price increases for off-patent drugs that have not undergone meaningful, clinically relevant improvements. In the meantime, the FDA's recent plan to accelerate generic drug approvals in markets with insufficient competition is encouraging,⁶ but along with other federal agencies, it should also consider the impact of market concentration when approving mergers or acquisitions.

Table 1 Characteristics of FDA-approved off-patent drugs in monopolistic or duopolistic markets

Characteristic	Total (n = 67)	0 generics (n = 44)	1 generic (n = 23)
Acquisition status			
Acquired at least once since 2000	37 (55)	27 (61)	10 (43)
Not acquired since 2000	30 (45)	17 (39)	13 (57)
Approved for rare disease ^a			
Orphan Designation	15 (22)	12 (27)	3 (13)
No designation	21 (31)	8 (18)	13 (57)
WHO essential medicine			
Included	18 (27)	14 (32)	4 (17)
Not Included	49 (73)	30 (68)	19 (83)
Therapeutic class			
Cancer	12 (18)	10 (23)	2 (9)
Cardiovascular, diabetes, or hyperlipidemia	7 (10)	3 (7)	4 (17)
Gastrointestinal	9 (13)	7 (16)	2 (9)
Infectious disease	13 (19)	8 (18)	5 (22)
Neurology/psychiatry	8 (12)	3 (7)	5 (22)
Other	18 (26)	13 (29)	5 (22)
Approval year			
1939–1962	13 (19)	10 (23)	3 (13)
1963–1984	20 (30)	15 (34)	5 (22)
1985–present	34 (51)	19 (44)	15 (65)

^aOrphan status designation began in 1983, so the number of orphan vs. non-orphan designated drugs differs from the total number of drugs
FDA Food and Drug Administration, WHO World Health Organization

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Author contributions All authors were responsible for the conception and design of this work. Dr. Gupta and Dr. Ross drafted the manuscript. Dr. Gupta conducted the statistical analysis. Dr. Gupta and Ms. Henkel were responsible for acquisition of data. Dr. Ross provided supervision. All authors participated in the interpretation of the data and critically revised the manuscript for important intellectual content.

Compliance with ethical standards:

Conflict of interest: Dr. Gupta is supported by the Yale University-Mayo Clinic Center of Excellence in Regulatory Science and Innovation (CERSI). The analysis presented in this paper was completed while Ms. Henkel was an undergraduate at Yale University and was included in her unpublished senior thesis in 2017. She has since graduated from Yale University and is now employed by Morgan Stanley. In the past 36 months, Dr. Ross has received research support through Yale University from Johnson and Johnson to develop methods of clinical trial data sharing, from Medtronic, Inc. and the Food and Drug Administration (FDA) to develop methods for postmarket surveillance of medical devices (U01FD004585), from the Food and Drug Administration to establish Yale-Mayo Clinic Center for Excellence in Regulatory Science and Innovation (CERSI) program (U01FD005938), from the Blue Cross Blue Shield Association to better understand medical technology evaluation, from the Centers of Medicare and Medicaid Services (CMS) to develop and maintain performance measures that are used for public reporting, from the Agency for Healthcare Research and Quality to examine community predictors of healthcare quality (R01HS022882), and from the Laura and John Arnold Foundation to establish the Good Pharma Scorecard at Bioethics International and to establish the Collaboration for Research Integrity and Transparency (CRIT) at Yale. Dr. Forman has no conflicts of interest to disclose.

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