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How Abbott's Fenofibrate Franchise Avoided Generic Competition

Nicholas S. Downing, AB, Joseph S. Ross, MD, MHS, Cynthia A. Jackevicius, PharmD, MSc, and Harlan M. Krumholz, MD, SM

Yale University School of Medicine, New Haven, Connecticut (NSD); Section of General Internal Medicine (JSR), Section of Cardiovascular Medicine and the Robert Wood Johnson Clinical Scholars Program (HMK), Department of Internal Medicine, Yale University School of Medicine; Yale–New Haven Hospital Center for Outcomes Research and Evaluation, New Haven, Connecticut (JSR, HMK); Section of Health Policy and Administration, Yale University School of Public Health, New Haven, Connecticut (HMK); and Western University of Health Sciences, Pomona, California and Institute for Clinical Evaluative Sciences, University of Toronto and University Health Network, Toronto, Ontario, Canada (CAJ)

Abstract

The ongoing debate concerning the efficacy of fenofibrate has overshadowed an important aspect of the drug's history: Abbott, the maker of branded fenofibrate, has produced several bioequivalent reformulations, which dominate the market even though generic fenofibrate has been available for almost a decade. This continued use of branded formulations, which cost twice as much as generic versions of fenofibrate, imposes an annual cost of approximately \$700 million on our healthcare system. Abbott maintained its dominance of the fenofibrate market, in part, through a complex switching strategy involving the sequential launch of branded reformulations that had not been shown to be superior to the first generation product and patent litigation that delayed the approval of generic formulations. The small differences in dose of the newer branded formulations prevented substitution with generics of older generation products. As soon as direct generic competition seemed likely at the new dose level where substitution would be allowed, Abbott would launch another reformulation and the cycle would repeat. Our objective, using the fenofibrate example, is to describe how current policy can allow pharmaceutical companies to maintain market share using reformulations of branded medications without demonstrating the superiority of next generation products.

INTRODUCTION

The efficacy of fenofibrate has been closely scrutinized in light of several studies that suggest that the lipid-modifying drug does little to reduce the risk of cardiovascular disease.^{1, 2} While the National Cholesterol Education Program guidelines recommend fibrate use in conjunction with a statin for certain patients whose triglycerides exceed 200 mg/dL, a more recent American Heart Association statement suggests that fibrates be restricted to those with triglycerides above 500 mg/dL.^{3, 4} Despite conflicting guidelines and

Corresponding author: Harlan M. Krumholz, MD, SM, 1 Church Street, Suite 200, New Haven, CT 06510, (203)-764-5885, (203)-764-5653 (fax), harlan.krumholz@yale.edu.

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questions about the drug's effectiveness in reducing cardiovascular risk, fenofibrate use has grown rapidly.⁵

Another aspect of this story is that in the United States, in contrast to Canada, there has been a remarkable persistence in the use of branded formulations, which generate almost \$1.4 billion in sales annually, over generics.^{5, 6} Typically a branded drug is rapidly marginalized soon after generics become available. For example, a recent analysis predicted that the market share of branded atorvastatin (Lipitor) would be effectively eliminated less than one year after generic versions of the drug are launched.⁷ In contrast, branded formulations account for the vast majority of fenofibrate prescriptions in the U.S. today, even though comparable generics have been available since 2002.⁵ This continued use of branded products causes substantially higher drug costs: if all patients taking branded formulations (i.e., those that contribute to the \$1.4 billion sales figure) switched to generic fenofibrate, which is half the price of the branded drugs, our healthcare system could realize annual savings of approximately \$700 million.^{6, 8, 9}

Abbott's commercial success can be explained, in part, by its complex switching strategy involving the sequential launch of branded reformulations of fenofibrate and patent litigation that delayed the approval of generics. The branded reformulations, which had no demonstrated incremental benefit on surrogate or patient outcomes (actually none of the formulations have been shown to improve patient outcomes), obtained significant market share while generic drug makers sought to resolve the patent litigation with Abbott that was delaying the approval of their products. Small differences in dose prevented substitution of newer branded reformulations with older generics. As soon as direct generic competition seemed likely with the latest formulation where substitution would be allowed, Abbott would launch another reformulation and the cycle would repeat.

In this article, we describe how Abbott's switching strategy fostered the continued use of branded reformulations of fenofibrate even though the company has faced generic competition for almost a decade and did not produce evidence that its reformulations were superior. This example highlights how current policy allows pharmaceutical companies to maintain market share of branded medications without demonstrating the superiority of next generation products.

THE FIBRATE DRUG CLASS

Fibrates are a class of medications that target genes involved in lipid metabolism.¹⁰ Since their discovery in the 1960s, several different fibrate drugs have been developed. The relevance of the earlier fibrates – clofibrate and gemfibrozil – to practice today is limited: clofibrate is no longer available in the U.S. while gemfibrozil has a small market share, likely because of its association with rhabdomyolysis, a potentially fatal muscle toxicity, when given with a statin.^{11, 12}

Fenofibrate, the most commonly used medication in the class, was developed by Fournier Laboratories in the 1980s.¹³ The company's first new drug application (NDA) was rejected in 1984. In its review, the Food and Drug Administration (FDA) noted that fenofibrate's efficacy, measured by observing surrogate endpoints not cardiovascular outcomes, was insufficient to offset the risk of adverse events observed in trials of clofibrate.¹³ Fenofibrate was eventually approved in 1993 on the basis of its triglyceride-lowering properties. Fournier never marketed the drug in the U.S.; instead, it licensed the rights to Abbott, which launched the drug branded as Tricor in 1998. Since then, fenofibrate has been reformulated several times at slightly different doses and has been approved for lowering low-density lipoprotein (LDL) and raising high-density lipoprotein (HDL) (Figure 1).^{14–18} More

recently, Abbott has launched fenofibric acid (Trilipix), a metabolite of fenofibrate, which can be used concomitantly with a statin.

In the U.S., fibrate utilization doubled in the 7-year period ending December 2009.⁵ Sales of Abbott's fibrate franchise follow a similar upward pattern that track its expanding number of approved indications (Figure 1). The publication of a large outcomes trial in 2005 showing that fenofibrate had little effect on cardiovascular outcomes did not slow sales growth.⁵ Sales of Abbott's fibrate franchise eclipsed 1 billion in 2006 and are expected to reach almost \$1.4 billion in 2011.^{6, 15}

PROTECTING FENOFIBRATE'S MARKET EXCLUSIVITY

Market exclusivity concepts and the generic drug approval process

Branded drugs are usually protected from competition for several years after approval, allowing their prices to be set at almost any level, in order to reward drug makers for their investment in the research and development process. Patent protection and data exclusivity work together to do this, as detailed in e-Appendix 1. Novel drugs are typically granted a data exclusivity period, which prevents others from using the clinical data generated by the drug's originator, thus precluding generic applications. Once the data exclusivity period expires, generic drug makers can submit an abbreviated new drug application (ANDA) that relies on the original data as long as these applications do not infringe upon the branded drug maker's patents. Alternatively, generic drug makers can challenge remaining patents by making a special certification in their ANDAs (e-Appendix 1). In this case, a branded drug maker typically responds by filing lawsuits that assert that the ANDAs infringe upon its intellectual property. By law, this action requires the FDA to delay approval of the ANDAs by up to 30 months to give the legal system an opportunity to resolve the dispute, meaning that the branded drug maker remains protected from generic competition during this time. If, after 30 months, litigation is still ongoing, the FDA approves the ANDA by default. This allows generics to be launched "at-risk": generic drug makers can sell generics but risk paying substantial damages if they are found in violation of the branded drug maker's patents.

Generic drug makers sought to copy Tricor-1 soon after launch

The original formulation of fenofibrate (Tricor-1) became susceptible to generic applications soon after its launch because most of its data exclusivity period was consumed by the delay between its approval (in 1993) and launch (in 1998). By February 2000, Novopharm, a generic drug maker, had filed an ANDA challenging a patent used in the manufacture of Tricor-1. Abbott rapidly responded by filing a patent infringement suit, which legally delayed the approval of this ANDA by 30 months or until the litigation was resolved, thus protecting Tricor-1 from competition (e-Appendix 2). Eighteen months later, Abbott won approval for a new formulation (Tricor-2) while its litigation with Novopharm, which had been acquired by Teva, remained unresolved. Consequently, Tricor-2 did not face generic competition at launch (Figure 2). The approval of Tricor-2, a branded reformulation of Tricor-1, was based solely upon bioequivalence studies showing that the new 54mg and 160mg tablets had the same pharmacologic properties as the original formulation of 67mg, 134mg and 200mg capsules (Table). No clinical trials involving Tricor-2 were submitted in this NDA.¹⁹

Tricor-2 rapidly replaced Tricor-1

Six months after approval, Tricor-2 accounted for 97% of fenofibrate prescriptions.⁹ Although it is not entirely clear how this switch was facilitated, antitrust lawsuits alleged that Abbott stopped detailing Tricor-1 and destroyed its inventory of the drug (e-Appendix

2). In addition, other pricing, marketing and promotional actions may have played a role. Nevertheless, a switch to a next generation drug was accomplished before a generic of the first generation was approved. Soon, a judge granted summary judgment in favor of Teva, paving the way for generic Tricor-1. However, this generic was unable to challenge Tricor-2's dominance because Tricor-2 could not be substituted for generic Tricor-1 because of differences in dose between the formulations, even though FDA approval of Tricor-2 was largely based on its bioequivalence data with Tricor-1. Unlike branded drug makers, generic drug makers do not have extensive sales forces. Instead, they rely on pharmacists, as well as physicians and payors, to switch patients from more expensive branded drugs to their generics. Most states have laws that require pharmacists to inform patients filling prescriptions for branded drugs when a generic is available and to ask their consent to dispense the generic.^{20, 21} In some states, this switching process is mandatory unless the prescriber specifically requests the branded drug. However, the minor dose difference between Tricor-2 and generic Tricor-1 meant that generic drug makers were unable to benefit from these regulations because pharmacists are not permitted to change the dose when substituting a generic for a branded drug.²⁰

Generic Tricor-2 and the development of a third formulation

Since Tricor-2 was approved on the basis of bioequivalence studies only, it was ineligible for data exclusivity, meaning that generic drug makers could immediately attempt to launch generic versions by challenging Abbott's patents. Teva, undeterred by its earlier experience, as well as Impax Laboratories, submitted ANDAs for generic Tricor-2 in late 2002. Abbott rapidly filed patent infringement complaints, thus postponing the approval of these ANDAs for as long as 30 months or until the litigation was resolved. Later in 2003, Abbott sued another generic drug maker, Ranbaxy, in response to another ANDA seeking to produce generic Tricor-2. Meanwhile Abbott continued to develop a new formulation of fenofibrate (Tricor-3) at slightly different doses than earlier versions (Table). Again, Abbott used bioequivalence studies that linked its new formulation back to clinical trials of Tricor-1 as the basis of its NDA. This new formulation had a small convenience claim: it could be taken anytime, while Tricor-1 and Tricor-2 were supposed to be taken with food. This claim, however, was based upon Tricor-3 meeting specific bioavailability criteria in pharmacodynamics studies of patients taking the drug in the fasting state.²² Abbott did not submit any comparative studies demonstrating the superiority of Tricor-3 over its earlier formulations for this claim.

Tricor-3 quickly replaced Tricor-2

Generic Tricor-2 was not available when Tricor-3 was approved in November 2004 because the patent infringement litigation had not been resolved.²² Patients were rapidly converted to Tricor-3; anti-trust lawsuits alleged Abbott used similar tactics to the earlier switch to drive uptake of its new reformulation (e-Appendix 2). By whatever means it occurred, the end result was that less than 70 days after Tricor-3's approval, Abbott reported that 70% of patients had been switched, and by the time generic versions of Tricor-2 were eventually approved in May 2005, 96% of fenofibrate prescriptions were written for Tricor-3.^{9, 16} The new doses of Tricor-3 would again prevent pharmacists from switching patients to Tricor-1 or Tricor-2 generics, presumably explaining why generics only accounted for 2.2% of all fenofibrate prescriptions at the end of 2006.⁹

The launch of Trilipix extended fenofibrate's market exclusivity through 2011

In December 2007, just before Teva filed an ANDA for generic Tricor-3, Abbott submitted an NDA for its fourth formulation, which it branded as Trilipix.²³ Aside from changing the dosing and switching back to a capsule formulation, Abbott changed the active ingredient from fenofibrate to fenofibric acid, a metabolite of fenofibrate. Trilipix's own NDA

demonstrates the similarity between these two drugs by presenting bioequivalence studies comparing Trilipix to Tricor-1.²³ Abbott also performed clinical trials measuring surrogate markers like HDL, LDL and triglycerides to demonstrate Trilipix's efficacy when combined with a statin.²³ According to FDA statutory requirements, Trilipix was granted a 3-year period of data exclusivity, which lasted until December 2011, despite similarities with earlier formulations and limited outcomes data supporting fibrate use.²⁴ Meanwhile, Abbott's litigation with Teva continued. Although the lawsuit was ultimately resolved in November 2009, a year after Trilipix was approved, Teva has not yet launched a generic version of Tricor-3.¹¹ Other companies' efforts to disrupt Abbott's fibrate franchise by launching various fenofibrate generics and branded generics have had limited success. In December 2009, Abbott's fibrate franchise accounted for 77% of all fenofibrate prescriptions and 58% of the fibric acid derivatives market.⁹

IMPLICATIONS OF FENOFIBRATE'S PROLONGED EXCLUSIVITY

Cost consequences

There is no evidence that Abbott's successive reformulations of fenofibrate have improved patient outcomes. Abbott's NDAs presented bioequivalence studies, not comparative data that demonstrated the benefit of its next generation products. However, these reformulations have imposed a substantial cost on our healthcare system by slowing the uptake of cheaper generics. The annual cost savings from switching all branded fenofibrate users to generic formulations, could exceed \$700 million.^{6, 8, 9}

Legal fallout

Abbott's strategy did not go entirely unnoticed. In May 2005, the Louisiana Wholesale Drug Company filed a class action lawsuit against Abbott, on behalf of all pharmacies and wholesalers that purchased Tricor, alleging the company's "unlawful exclusion of competition from the market for fenofibrate" (e-Appendix 2). Abbott was also the subject of a similar antitrust complaint brought by various Tricor patients. Both lawsuits cite the same sequence of events described in this paper as evidence that Abbott violated the Sherman Act, which outlaws monopolies and any effort to establish such market position. Abbott was sued again in 2008 by 19 different states, which made similar allegations to those of the plaintiffs in the earlier lawsuits but also highlighted their view that Abbott had broken various state antitrust laws. Ultimately, Abbott settled each of these lawsuits at a combined cost to the company of over \$300 million, which amounts to less than 4% of total sales to date of Abbott's fibrate franchise (e-Appendix 2).

POLICY IMPLICATIONS

We believe that various stakeholders, namely payors, physicians, pharmacists, patients, and lawmakers, can act to ensure that market exclusivity and premium prices are reserved for real innovations that improve patient outcomes. Since the pharmaceutical industry may be influenced by its investors' focus on profitability, and this strategy contributed to Abbott's profits, external encouragement may help focus industry's research and development efforts on innovations that improve patient care rather than reformulations lacking demonstrated benefits over original drugs. In this section, we discuss how various stakeholders could reduce the attractiveness of similar switching strategies, thereby challenging industry to demonstrate the value of its next generation products over the prior generation or be forced to face generic competition.

FDA and Federal lawmakers: Eliminate the moral hazard of the 30-month stay

The 30-month stay of ANDA approvals, triggered by Abbott's patent infringement lawsuits, created a critical delay between the launch of Abbott's new formulations and the approval of generics of older fenofibrate formulations. This delay facilitated uptake of Abbott's branded reformulations because they faced no generic competition. The FDA could require that all drug makers seeking approval for NDAs involving a new formulation or dose of a previously approved molecule resolve any outstanding patent infringement lawsuits concerning the original drug before their application is approved. Such a law would allow the FDA to approve these NDAs at the same time as ANDAs involving older formulations. (Currently, decisions about these generic applications are delayed by the 30-month stay.) Establishing a mechanism that approves branded reformulations and generics simultaneously would allow drug makers to compete for patients on a level playing field. If the formulations are equivalent, then the price will determine the choice. If a new formulation offers a demonstrated advantage, then it may justify a higher price. In this approach, branded drug makers are protected from invalid challenges to their intellectual property because the original formulation's exclusivity is preserved until the litigation has been resolved and the new branded drug is approved. Judges have the authority to reduce the length of the 30-month stay, thus limiting the risk that branded drug makers will attempt to obstruct the legal process.

FDA and federal lawmakers: Alert other stakeholders of reformulations

Abbott's subtle reformulations were somewhat obscured by the company's ability to retain the Tricor brand name for its first three formulations of fenofibrate. In contrast, Abbott changed its Canadian brand name with each reformulation, clearly signaling to other stakeholders that the drug had been modified. The FDA could help raise awareness of reformulations if the law required that branded drug makers market their reformulations under different brand names.

Patients and payors: Demand cost-effective treatments

The commercial success of fenofibrate is even more remarkable given that only Trilipix, and to a lesser extent, Tricor-1, enjoyed data exclusivity, which provides complete protection from generic competition. The strength of Abbott's fibrate franchise in the absence of such protection suggests that regulatory changes could be of modest benefit. While there is little that patients and payors could have done to promote generic competition for fenofibrate, these stakeholders were well positioned, as the pharmaceutical industry's customers, to challenge the high price of Abbott's drugs. In a similar drug class, payors have used the availability of generics to extract discounts from branded drug makers: ExpressScripts, a large pharmacy benefit manager (PBM), removed atorvastatin, the world's best-selling drug, from its formulary for several months in 2006 because of a price dispute when generic versions of simvastatin, a related LDL-lowering drug, became available.²⁵ Eventually ExpressScripts won concessions from Pfizer, thus highlighting the increasing influence of payors and PBMs in determining drug costs. Interestingly, Tricor-3 continues to command a premium price even though many generics are available, suggesting that such cost-effectiveness calculations are not currently employed systematically.⁸

The French approach to setting prices for new drugs provides an interesting case study. It incorporates an assessment of a drug's innovation and incremental benefit, which is directly linked to the drug makers' ability to name their own price.^{26, 27} Although our healthcare system has avoided price regulation, payors could consider a similar approach when negotiating drug prices. This would inform formulary position and translate into changes in copayment level, thus empowering patients and physicians to determine if a drug's demonstrated benefits are worth additional cost. Payors could mitigate concerns about

rationing by applying this value-based calculus to reformulated drugs only. Few payors appear to have adopted this strategy: Trilipix has a low copayment level on several leading formularies.²⁸

Pharmacists and state lawmakers: Facilitate generic switching at bioequivalent doses

The inability of pharmacists to switch patients with prescriptions for the new reformulations to generics prevented meaningful uptake of these less expensive drugs. Even though Abbott conducted bioequivalence trials that showed that its reformulations had the same effects as Tricor-1, pharmacists were unable to switch patients because of dose differences between each of the Tricor formulations. Revising the language of generic substitution statutes to allow switching between bioequivalent drug formulations (including those at different doses) could prevent the recurrence of similar switching strategies. Such an approach would require careful consideration of bioequivalence criteria, which mandate that the pharmacokinetic properties of a generic drug fall within a certain range relative to those of the original drug. Drugs like fenofibrate, which have large therapeutic windows, can be safely substituted with bioequivalent formulations. However, the substitution of other drugs, such as warfarin, with bioequivalent preparations could compromise patient safety because there is a much smaller difference between effective and toxic doses. Consequently, any attempt to promote switching between different yet bioequivalent formulations of the same drug must carefully balance potential safety risks. The challenge of setting appropriate bioequivalence criteria has been highlighted by current efforts to formalize the approval process for “biosimilars” (generic versions of biologic drugs). Also, generic substitution laws are set by the states, so such an approach would require substantial legislative efforts at the State level.

Physicians: Take responsibility for cost-effective care

The fenofibrate example is also a cautionary tale for physicians who must accept some responsibility for the continued use of branded fenofibrate. Despite the availability of many fenofibrate generics over the past 9 years, physicians have continued to prescribe Abbott’s more expensive formulations, which accounted for over 75% of all fenofibrate prescriptions in December 2009.^{5, 9} Physicians should be prepared to question minor dosing changes to branded drugs. In this example, physicians could have asked for data demonstrating the benefit of each reformulation or why fenofibrate’s dosing was repeatedly changed. Admittedly, Abbott’s switching strategy left them little choice until the generic versions were approved. Improvements in information systems, such as electronic medical records and drug databases, could be used to highlight the availability of comparable or bioequivalent generic drugs. Even if such improvements are made, physicians make the ultimate prescribing decision and must take responsibility for providing the highest quality of care, at reasonable cost, for patients.

CONCLUSION

While we have used Abbott’s handling of fenofibrate as an illustrative example of a branded drug maker maintaining a dominant market share years after generic competition was permitted, it is only one example. However there are other instances of similar strategies: AstraZeneca’s efforts to switch patients from omeprazole (Prilosec) to the active enantiomer of the old drug, esomeprazole (Nexium), in 2001 is well documented.²⁹ Such strategies are particularly worrying given concerns about the unsustainable growth of healthcare costs. Fortunately, this is a solvable problem, as small changes to the current regulations and structure of our healthcare system have the potential to foster appropriate generic competition and ensure that drug makers demonstrate the value of their next generation products.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Keech A, Simes RJ, Barter P, et al. Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. *Lancet*. 2005; 366:1849–1861. [PubMed: 16310551]
2. Ginsberg HN, Elam MB, Lovato LC, et al. Effects of combination lipid therapy in type 2 diabetes mellitus. *N Engl J Med*. 2010; 362(17):1563–1574. [PubMed: 20228404]
3. National Heart Lung and Blood Institute. [Accessed December 20, 2011] Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Cholesterol in Adults (Adult Treatment Panel III). http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm
4. Miller M, Stone NJ, Ballantyne C, et al. Triglycerides and cardiovascular disease. *Circulation*. 2011; 123(20):2292–2333. [PubMed: 21502576]
5. Jackevicius CA, Tu JV, Ross JS, Ko DT, Carreon D, Krumholz HM. Use of fibrates in the United States and Canada. *JAMA*. 2011; 305(12):1217–1224. [PubMed: 21427374]
6. Lewis, DR.; Beuchaw, S.; Francescone, J.; Demchick, JL. Morgan Stanley Research North America. Morgan Stanley; 2011. Abbott Laboratories - Three ways to spin.
7. Jackevicius, CA.; Chou, MM.; Ross, JS.; Shah, ND.; Krumholz, HM. [Accessed December 23, 2011] Generic atorvastatin and health care costs. *New Engl J Med* (online first). <http://www.nejm.org/doi/full/10.1056/NEJMp1113112>
8. [Accessed Sept 7, 2011] Tricor - Drugstore.com. <http://www.drugstore.com/tricor/145mg-tablets/qxn00074612390>
9. IMS Health-US. National Prescription Audit.
10. Fruchart JG, Staels B, Dallongeville J, Auwerx J, Schoonjans K, Leitersdorf E. Mechanism of action of fibrates on lipid and lipoprotein metabolism. *Circulation*. 1998; 98(19):2088–2093. [PubMed: 9808609]
11. Food and Drug Administration. [Accessed Sept 7, 2011] Drugs@FDA. <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>
12. Graham DJ, Staffa JA, Shatin D, et al. Incidence of hospitalized rhabdomyolysis in patients treated with lipid-lowering drugs. *JAMA*. 2004; 292(21):2585–2590. [PubMed: 15572716]
13. Food and Drug Administration. [Accessed Sept 7, 2011] Label and Approval History: Lipidil (fenofibrate); Application No.: 019304. http://www.accessdata.fda.gov/drugsatfda_docs/nda/pre96/019304_s000.pdf

14. Lewis, DR.; Beuchaw, S.; Francescone, J. Morgan Stanley Research North America. Morgan Stanley; 2011. Abbott Laboratories - Double digit growth in search of a multiple.
15. Reicin, G.; Miksic, M.; Roman, DH. Morgan Stanley Research North America. Morgan Stanley; 2008. Abbott Laboratories - 4Q07: Good quarter; we remain buyers.
16. Reicin, G.; Miksic, M.; Yik, A. Equity Research North America. Morgan Stanley; 2005. Abbott Laboratories - 4Q04: Strong top line offsets TAP adjustments.
17. Reicin, G.; Wittes, J. North America Equity Research. Morgan Stanley Dean Witter; 2001. Abbott Laboratories - ABT: 4Q00 a solid performance.
18. Reicin, G.; Wittes, J.; Miksic, M. Equity Research North America. Morgan Stanley; 2003. Abbott Laboratories - 4Q02: Issues are now on the table; upgrading the stock.
19. Food and Drug Administration. [Accessed Sept 7, 2011] Drug Approval Package: Tricor (fenofibrate) Tablets; Application No.: 021203. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2001/21-203_Tricor.cfm
20. State regulations on generic substitution. Pharmacist's Letter/Prescriber's Letter. 2006; 22(9): 220901.
21. Vivian J. Generic-substitution laws. US Pharm. 2008; 33(6):30–34.
22. Food and Drug Administration. [Accessed Sept 7, 2011] Drug Approval Package: Tricor (Fenofibrate) Tablets; Application No.: 021656. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2004/021656s000_TricorTOC.cfm
23. Food and Drug Administration. [Accessed Sept 7, 2011] Drug Approval Package: Trilipix (fenofibric acid) Delayed Release Capsules, 45 mg, 135 mg; Application No.: 022224. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2008/022224_trilipix_toc.cfm
24. Food and Drug Administration. [Accessed Sept 7, 2011] Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations (current through July 2011). <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>
25. Rapaport, L.; Larkin, C. [Accessed Sept 8, 2011] Express Scripts Restores Coverage of Pfizer's Lipitor (Update5). <http://www.bloomberg.com/apps/news?pid=newsarchive&sid=a5eA4WftkjzU&refer=healthcare>
26. Haute Autorité de Santé. [Accessed Sept 8, 2011] Outlook and challenges for the future: A French perspective. <http://www2.lse.ac.uk/businessAndConsultancy/LSEConsulting/conferences/meyer.pdf>
27. Office of Fair Trading. [Accessed Sept 8, 2011] Annexe K: International Survey of Pharmaceutical Pricing and Reimbursement Schemes. http://www.oft.gov.uk/shared_oftr/reports/comp_policy/oft885k.pdf
28. Fingertip Formulary. [Accessed July 1, 2011] <http://www.fingertipformulary.com>
29. Angell, M. The truth about drug companies: how they deceive us & what to do about it. New York: Random House; 2004.

Figure 1.
Sales and indications of Abbott's fenofibrate franchise.^{14–18}

Figure 2.
Evolution of Abbott's fenofibrate franchise relative to generic competition.

Table

Summary of the formulations of fenofibrate. 13, 19, 22, 23

Brand name (active ingredient)	Dosing and formulation	Basis of FDA approval	Notable outcomes trials
Tricor-1 (fenofibrate)	67mg, 134mg, 200mg capsules	Clinical trials demonstrating the drug's effect on triglycerides and low-density lipoprotein	Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study, 2005: Fenofibrate did not reduce rate of cardiovascular events
Tricor-2 (fenofibrate)	54mg, 160mg tablets	Bioequivalence studies that show that Tricor-2 = Tricor-1 Analysis of old Tricor-1 data to support inclusion of high-density lipoprotein-lowering claims in the label No clinical trials	Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, 2010: Fenofibrate did not reduce rate of cardiovascular events
Tricor-3 (fenofibrate)	48mg, 145mg tablets	Bioequivalence studies that show that Tricor-3 = Tricor-1 No clinical trials	None
Trilipix (fenofibric acid)	45mg, 135 mg "delayed release" capsules	Bioequivalence studies that show that Trilipix = Tricor-1 Clinical trials to support the combination therapy indication	None