

how they are used. Professional medical societies or an organization such as Consumers Union could develop reporting standards, and the Department of Health and Human Services could consider adding transparency requirements to the “meaningful use” criteria for EHR certification. Greater transparency would also facilitate research on the prevalence of digital marketing activities and quantification of their influence on clinical practice.

Second, recognizing that actions on social media sites are monitored, physicians could exercise the same caution with regard to interactions with promotional materials online as they do with sales representatives offline. Similarly, reporting of physician payments originating from these sites (through paid surveys or the Sermo “Challenges,” for instance) could be mandated under the Physician Payments Sunshine Act. Currently, many of these payments are not reported because they are made through third parties rather than directly by manufacturers.

Third, professional societies could issue guidelines calling for firewalls to keep marketing out of patient visits — as they did with free pens and other traditional marketing tools — and the Code on Interactions with Health Care Professionals used by the Pharmaceutical Research and Manufacturers of America could be similarly amended. At a minimum, professional societies could increase physicians’ awareness of these new marketing practices, which are often deployed in ways that physicians may not recognize as marketing. Physician leaders could, in turn, begin discussions within their practices about discouraging use of technologies that embed marketing into patient care when other options exist. As with EHRs, independent evaluations of mobile applications can guide physicians to applications that do not allow marketing.

Digital technology is changing the nature of marketing, and policies intended to limit its influence are lagging behind. But the medical profession can enact policies to ensure that patients,

not advertising, remain the focus of care.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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High-Cost Generic Drugs — Implications for Patients and Policymakers

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It is well known that new brand-name drugs are often expensive, but U.S. health care is also witnessing a lesser-known but growing and seemingly paradoxical phenomenon: certain older drugs, many of which are generic and not protected by

patents or market exclusivity, are now also extremely expensive. Take the case of albendazole, a broad-spectrum antiparasitic medication. Albendazole was first marketed by a corporate predecessor to GlaxoSmithKline (GSK) outside the United States in

1982 and was approved by the Food and Drug Administration (FDA) in 1996. Its patents have long since expired, but no manufacturer ever sought FDA approval for a generic version. One reason may be that the primary indications for the drug — in-

testinal parasites, neurocysticercosis, and hydatid disease — occur relatively rarely in the United States and usually only in disadvantaged populations such as immigrants and refugees. In late 2010, the listed average wholesale price (AWP) for albendazole was \$5.92 per typical daily dose in the United States and less than \$1 per typical daily dose overseas.

By 2013, the listed AWP for albendazole had increased to \$119.58 per typical daily dose.¹ We found that at some pharmacies in Minnesota, an uninsured patient requiring 6 months of treatment would have faced costs amounting to tens of thousands of dollars.¹ Although the AWP may not reflect the actual cost of the product, Medicaid data show that spending on albendazole increased from less than \$100,000 per year in 2008, when the average cost was \$36.10 per prescription, to more than \$7.5 million in 2013, when the average cost was \$241.30 per prescription (see graph).

The albendazole story is not unique. According to the National Average Drug Acquisition Cost pricing file, the price of captopril (12.5 mg), which is used for hypertension and heart failure, increased by more than 2800% between November 2012 and November 2013, from 1.4 cents to 39.9 cents per pill. Similarly, the price of clomipramine (25 mg), a long-established tricyclic antidepressant also used for obsessive-compulsive disorder, increased from 22 cents to \$8.32 per pill, and the price of doxycycline hyclate (100 mg), a broad-spectrum antibiotic that has been around since 1967, increased from 6.3 cents to \$3.36 per pill.²

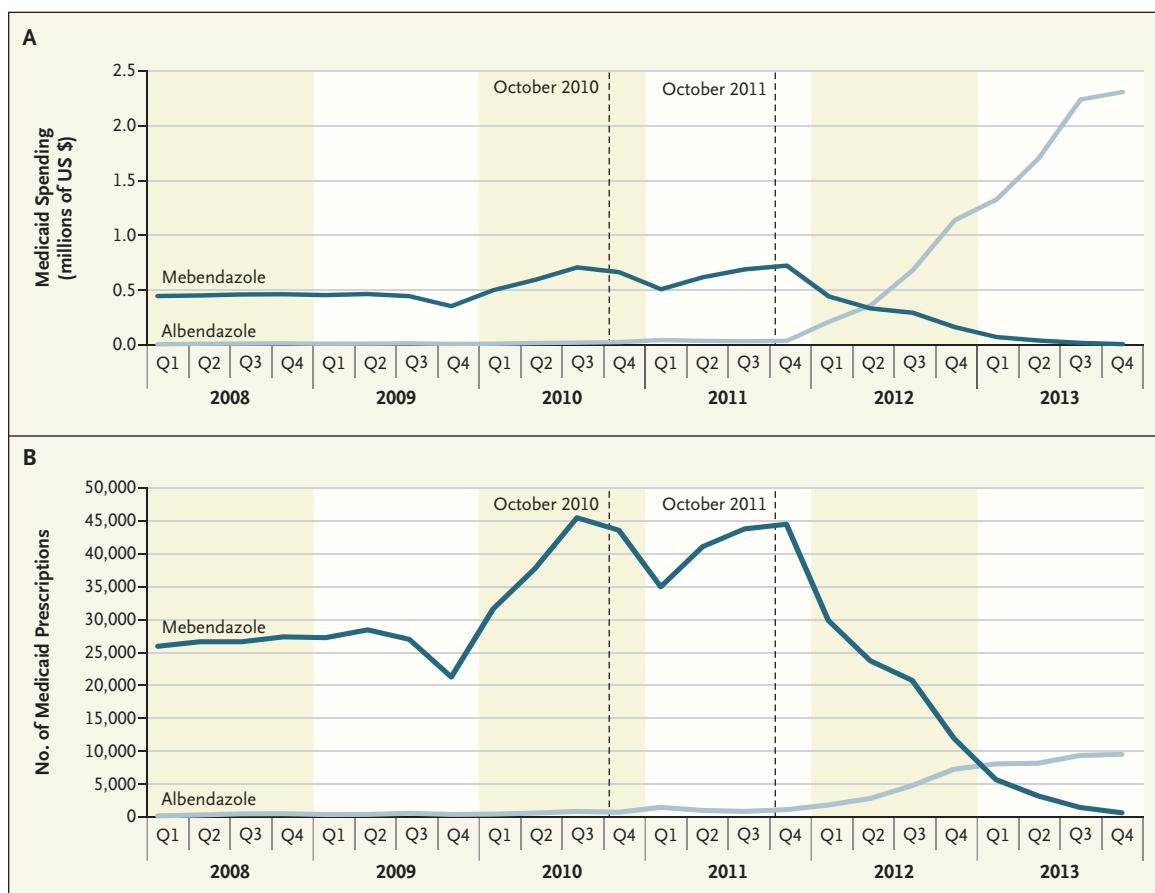
Yet many of these drugs remain key therapeutic tools. The number of prescriptions for albendazole has increased dramatically, in part because the drug has increasingly been used to treat parasitic infections in refugees. The Centers for Disease Control and Prevention recommends presumptive treatment of refugees arriving in the United States if they have not had prior treatment. Because the people who need albendazole are generally disadvantaged, the costs resulting from the enhanced demand and associated price increases are largely borne by the patients themselves through substantial out-of-pocket payments or by taxpayers through public insurers such as Medicaid and the Refugee Medical Assistance program.

Numerous factors may cause price increases for non-patent-protected drugs, including drug shortages, supply disruptions, and consolidations within the generic-drug industry.³ These factors generally lead to a decrease in market competition. For example, between 2002 and 2013, some manufacturers of digoxin — which is still used for atrial fibrillation and heart failure — faced safety-related drug recalls and FDA inspections, and the number of manufacturers of oral digoxin (tablet) fell from eight to three. During that time, the drug's price reportedly increased by 637%. Similarly, the price increase for doxycycline was most likely exacerbated by a national shortage in 2013, which the FDA attributed to increased demand in the face of limited manufacturing capacity.

The case of albendazole reveals additional circumstances that may contribute to price in-

creases for older drugs. Although GSK continues to manufacture albendazole, the company sold its U.S. marketing rights to Amedra Pharmaceuticals, a small, private firm, in October 2010.⁴ In 2011, Teva Pharmaceuticals discontinued manufacturing of the only therapeutically interchangeable antiparasitic agent, mebendazole (Vermox), for non-safety-related business reasons, and prescribing of mebendazole slowed (see graph). Although many contributors to the price a manufacturer sets for a drug, such as shortages of raw materials or price mark-ups elsewhere along the pharmaceutical supply chain, are out of a particular manufacturer's control, Amedra's business strategy may be to corner a niche market for a pharmaceutical agent. Amedra has similarly acquired from GSK dextroamphetamine (Dexedrine Spansule), a treatment for attention-deficit disorder, and pyrimethamine (Daraprim), which is used to treat toxoplasmosis. The prices of both drugs increased after their acquisition, though to a lesser extent than albendazole's price.

Although high prices charged for albendazole and other drugs by manufacturers that hold a monopoly (or a near monopoly) on them can hinder access for certain patients, U.S. antitrust laws protect consumers only from anticompetitive strategies such as price fixing among competitors. Manufacturers of generic drugs that legally obtain a market monopoly are free to unilaterally raise the prices of their products. The Federal Trade Commission will not intervene without evidence of a conspiracy among competitors or other anticompetitive actions that sustain the increased



Medicaid Spending and Prescriptions for Albendazole and Mebendazole, 2008–2013.

In October 2010, GlaxoSmithKline sold U.S. marketing rights for albendazole to Amedra Pharmaceuticals. In October 2011, Teva Pharmaceuticals ceased to manufacture mebendazole. Data are from the Centers for Medicare and Medicaid Services.

price. Amedra did acquire albendazole's only near-term potential competitor, mebendazole, from Teva in 2013, though that move may not rise to the level of anti-competitive behavior.

When shortages of generic drugs have led to high prices, the FDA has responded by temporarily approving drug imports or working with domestic manufacturers to help increase production by helping to expedite companies' ability to integrate new raw-material resources into their production lines. The FDA may not be able to use the same mechanisms to address high prices of essential generic drugs that are

made by only one manufacturer. Instead, we believe that special pathways should be created to promote competition and permit the private market to function more efficiently. In the case of albendazole, the recent increases in both prescriptions and price may make the drug more attractive to other generics manufacturers and encourage them to produce their own versions. However, new generics manufacturers can experience delays before the FDA's Office of Generic Drugs approves their products. According to the FDA, the standard processing time for such applications is about 10 months,

which does not include the time it may take the manufacturer to address any deficiencies in its proposal. Legislation passed in 2012 created new generic-drug user fees that promise to reduce such waiting times by increasing funding for FDA staff.

In addition, substantial increases in the price of an unpatented drug could trigger the FDA to issue a public announcement seeking other manufacturers for generic versions of the product. Companies responding to such a request could receive expedited reviews of their manufacturing processes and bioequivalence data. Generic-drug user fees could be

waived in these circumstances to further increase incentives for potential competitors. Entry into the market of more generics manufacturers should increase competition and reduce prices. Of course, other players along the drug-distribution chain, such as wholesalers or pharmacies, may also contribute to price markups, and further investigation is needed into the relative contribution of these different actors to the high prices of drugs such as alendazole.

Meanwhile, there is little that individual consumers can do. Some drug companies, such as Amedra, offer assistance programs for indigent patients, but these programs often have complicated enrollment processes, and they do not offer an effective general safety net.⁵ Some patients

instead seek to acquire these drugs in other countries, since many of them are widely and inexpensively available outside the United States, but such foreign sources may be of variable quality. Until regulatory and market solutions are implemented to reduce prices for these older drugs, patients requiring such drugs and the physicians treating them will continue to be faced with difficult choices.

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Protecting Progress against Childhood Obesity — The National School Lunch Program

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Nutrition science has advanced greatly since the inception of the National School Lunch Program in 1946. Yet when a 2008 Institute of Medicine (IOM) committee comprising 14 child-nutrition experts examined data on the content of school lunches in the United States, its findings were stark. Children ate strikingly few fruits and vegetables, with little variety. Potatoes accounted for one third of vegetable consumption. Intake of refined grains was high. Almost 80% of children consumed more saturated fat than was recommended, and sodium intake was

excessive in all age groups. Children ate more than 500 excess calories from solid fats and added sugars per day.¹

In response to these findings, Congress enacted the Healthy, Hunger-Free Kids Act of 2010 (HHFKA), which called for a revision of school-nutrition standards. The updated standards aligned school meals with the 2010 Dietary Guidelines for Americans by increasing quantities of fruits, vegetables, and whole grains; establishing calorie ranges; and limiting trans fats and sodium (see diagram). The HHFKA also provided an incentive for schools to adhere

to the regulations: a much-needed increase in meal reimbursement. Implementation of the new standards has been proceeding gradually since 2012, and we have an unprecedented opportunity to improve the quality of meals consumed by U.S. children. Children consume almost half of their total calories at school, and the National School Lunch Program provides low-cost or free lunch to more than 31 million students at 92% of U.S. public and private schools.

But now, just 2 years after its implementation began, the HHFKA is at risk of being under-