

Limited Distribution Networks Stifle Competition in the Generic and Biosimilar Drug Industries

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Limited distribution networks (LDNs) are established when a drug manufacturer contracts with 1 or a limited number of drug distributors. LDNs can facilitate effective allocation of a drug by allowing the pharmaceutical company to more tightly manage the supply chain, minimize the impact of drug shortages, and reduce the amount of unused product in the supply chain. Manufacturers and some specialty pharmacies assert that restricting the number of drug distributors in a limited distribution model enables safe and effective drug delivery to small patient populations and allows for “high-touch care” that may include patient education, counseling, or instruction on administration techniques; data collection and reporting; and patient monitoring for adherence and adverse effects. Drug companies also benefit financially from savings on inventory management and distribution fees.¹ The traditional pharmaceutical supply chain is an open network in which a pharmaceutical company makes a drug broadly accessible through a distribution channel that usually includes 1 of the major wholesalers—AmerisourceBergen Corporation; Cardinal Health, Inc; or McKesson Corporation—and various dispensing pharmacies, including but not limited to retail, clinic, nursing home, hospital, mail order, and specialty pharmacies. LDNs, also referred to as limited distribution chains, closed distribution systems, controlled distribution systems, or restricted distribution systems, limit a drug’s distributors to 1 or a small number of select pharmacies or specialty wholesale distributors, often entirely circumventing the major pharmaceutical wholesalers.¹ We broadly define pharmaceutical distributor to include all parties that handle a drug between the manufacturer and the patient end user. LDNs composed of just 1 distributor are referred to as exclusive distribution networks (EDNs)²; this distribution strategy has the greatest anticompetitive impact because it accords the drug company the highest degree of control over distribution and sales.

Members of Congress became aware of LDNs when they investigated why some drug companies were able to raise prices on off-patent drugs and no competitors materialized. The US Senate

ABSTRACT

A limited distribution network (LDN) restricts the distribution channel for a pharmaceutical drug to 1 or a very small number of distributors. This strategy may allow for more effective allocation of drugs in shortage and is purported to help ensure the safe distribution of high-risk drugs to small patient populations. However, in recent years, some drug companies, including Turing Pharmaceuticals, have used LDNs to prevent generic and biosimilar companies from accessing samples of drug products necessary to perform testing required by the FDA for generic and biosimilar drug applications. LDNs also hamper provider access to pharmaceuticals and facilitate price gouging. This paper synthesizes existing knowledge on the misuse of LDNs to thwart competition, clarifies the relationship between limited distribution and the FDA Risk Evaluation and Mitigation Strategies, discusses proposed federal legislation under consideration to address this issue, and offers several policy options to remedy this anticompetitive practice, including authorizing the FDA to require the sale of approved drug products to generic and biosimilar drug developers.

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Special Committee on Aging found evidence from internal documents revealing the intentional use of LDNs by Turing Pharmaceuticals to thwart competition and accomplish price gouging: “Restricted distribution...was a deliberate part of Turing’s plan to defend its shocking price increase and subsequent increased revenue against potential competition.”³ The director of patient access at Turing Pharmaceuticals has commented that if a generic drug maker had sought to purchase Daraprim, the antiparasitic drug now well-known after its large price increase from \$13.50 to \$750 per pill, he would not have approved the purchase on the grounds that his company did not want to facilitate competition that could undercut the price of Turing’s drug.⁴ The former general counsel of Turing Pharmaceuticals testified before the US Senate Special Committee on Aging that “in the case of Daraprim, retention of a new specialty pharmacy distributor to carry on a closed distribution system was considered an integral part of the company’s desire to block a generic entrant for at least 3 years.”⁵ The Senate Aging Committee report found that other companies have used LDNs with a similar intent: to obstruct access to drug samples that are sought by competitor companies in order to conduct testing necessary to submit a generic or biosimilar drug application to the FDA.

LDNs and REMS

Some drug companies point to the FDA Risk Evaluation and Mitigation Strategies (REMS) as their primary rationale for creating an LDN or EDN. However, this ignores the facts that LDNs are not required as part of REMS and that many of the drugs with LDNs are not considered a great enough safety risk by the FDA to warrant REMS.

The Food and Drug Administration Amendments Act (FDAAA) of 2007 authorized the FDA to require a REMS for any drug or drug class that poses a serious safety risk. REMS are essentially risk management plans that help ensure that the benefits of high-risk drugs to patients outweigh their risks.⁶ REMS may contain 1 or more of several elements: a medication guide, a communication plan, elements to assure safe use (ETASU), and an implementation system. ETASU establish requirements for the drug’s safe distribution and dispensation, such as permissible locations for drug administration, prescriber training and certification, pharmacy training and certification, patient monitoring, and documentation of conditions for safe use.⁶ REMS may include an implementation system that places responsibility on the drug manufacturer to oversee the operation of ETASU and ensure their execution.

The manufacturer is obligated to construct and implement REMS in accordance with FDA requirements. Although REMS may require the sale of drug products only to named patients with a valid

TAKEAWAY POINTS

Drug companies employ limited distribution networks (LDNs) to obstruct access to drug samples sought by competitor companies in order to conduct testing necessary to submit a generic or biosimilar drug application to the FDA.

- ▶ The resulting delays in generic and biosimilar market entry translate to sizable lost savings for US payers and patients.
- ▶ A common misconception is that LDNs are required as part of FDA Risk Evaluation and Mitigation Strategies (REMS); in fact, they are not. Some drug companies nonetheless use REMS to justify access restrictions via LDNs.
- ▶ The FDA currently has no authority to compel drug companies to sell samples of drugs in LDNs to competitor companies.
- ▶ There are 2 bills currently under consideration in Congress to remedy the misuse of LDNs and REMS for anticompetitive purposes: the CREATES Act of 2017 and the FAST Generics Act of 2017.

prescription and may prohibit a product’s sale in retail pharmacies, the FDA neither recommends nor mandates a restriction on the number of pharmacy distributors as a means to achieve drug safety. As of March 2018, the FDA database of approved REMS contained 74 drugs,⁷ but our preliminary research of limited distribution drug lists made publicly available by specialty pharmacies suggests that more than 100 drugs have been placed in manufacturer-imposed LDNs. The number can change rapidly as drugs are included in LDNs.

When the FDAAA was enacted in 2007, Congress foresaw that REMS could be used to justify access restrictions. To address this potential problem, a provision of the FDAAA specifies that “no holder of an approved covered application shall use any element to assure safe use required by the Secretary [of HHS] under this subsection to block or delay approval” of abbreviated new drug applications (ANDAs) by drug developers.⁸ Despite the existence of this provision in the law, LDNs are being used to deter generic and biosimilar development and market entry.

Misuse of LDNs to Stifle Competition

The Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Act) expedites generic drug approval after the patent and market exclusivity periods end for branded drugs. To increase the level of competition between branded and generic drugs, the Hatch-Waxman Act established a simpler drug approval process, the ANDA, which eliminated the redundant preclinical and clinical trial testing for generic versions of an already approved branded drug, referred to as the Reference Listed Drug (RLD), in applications to the FDA. Instead, the FDA requires bioequivalence testing in order to demonstrate that the generic drug acts in the same manner in the human body as the RLD (ie, to “ensure therapeutic equivalence between a pharmaceutically equivalent test drug product and a reference listed drug”). Similarly, the Biologics Price Competition and Innovation Act of 2009 (BPCIA) amended the Public Health Service Act to facilitate abbreviated licensure of biosimilars, with requirements for testing

to establish that the biosimilar product does not differ from the FDA-licensed biologic product in a clinically meaningful way.¹⁰

For most drugs and biologics not in LDNs, generic companies simply purchase the RLD for bioequivalence testing on the free market, usually from pharmaceutical wholesalers. When there is an LDN, however, drug manufacturers contract with a select few distributors and may include in their contract terms specifications that a drug product be sold only to approved purchasers (such as individual patients with a valid prescription), thereby contractually prohibiting the distributor from selling samples to generic and biosimilar companies. In some cases, drug companies make explicit their efforts to obstruct competition via LDNs, thereby making it more difficult for the generic company to obtain the drug and compete in the marketplace. Bruce Leicher, senior vice president and general counsel of Momenta Pharmaceuticals, testified on behalf of the generic pharmaceutical industry in March 2017 before the House Committee on Oversight and Government Reform that “in our company’s development decision-making process, we are forced to consider how difficult it will be to obtain the brand product. In cases where access is restricted, we have not initiated some programs.”¹¹

The FDA is aware of this phenomenon, but it lacks the legal authority to compel a drug company to sell its drug to a potential competitor. Janet Woodcock, MD, director of the Center for Drug Evaluation and Research at the FDA, stated in the same March 2017 Congressional hearing that the FDA has no authority to compel drug companies to sell samples of drugs in limited distribution chains to competitor companies; the only action the FDA can take is to “notify the innovator in writing...that the REMS restriction does not apply” to the sale of samples to drug developers.¹² Yet, as Woodcock noted in her testimony, drug makers continue to withhold their drugs, and the FDA has received more than 150 inquiries from generic companies that have been unable to access drugs for bioequivalence testing.¹²

Generic companies are forced to engage in costly litigation in order to obtain samples. In some cases, brand drug companies have filed suit against generic companies to avoid providing access.¹³ Although it would seem possible to obtain the drugs through other routes, it is important for the generic or biosimilar company to be able to demonstrate that the drug was obtained through legitimate channels. One notable case relating to this issue, *Mylan Pharmaceuticals, Inc v Celgene Corp*, No. 2:14-CV-2094-ES-MAH (D NJ 2014), involved claims by generic drug maker Mylan that Celgene used REMS for 2 of its chemotherapeutic drugs as a pretext to withhold these drugs from developers like Mylan and so maintain unlawful monopolies. The Federal Trade Commission issued an amicus curiae brief in this case and maintains ongoing investigations into these practices.

Drug companies have also used REMS patents as an anticompetitive tactic to deter competition, even when the active ingredient of

the drug product is no longer patent protected. The drug company may patent drug-specific REMS processes and protocols (ie, ETASU). Under current law, the FDA is authorized only to “seek to negotiate a voluntary agreement” between the ETASU patent holder and the generic drug company.¹⁴ The Federal Food, Drug & Cosmetic Act, as amended by the FDAAA of 2007, contains 2 provisions that address whether the sponsor of an RLD may use a patent on the ETASU in a required REMS to hinder generic competition.^{8,14} These provisions neither resolve the issue of shared REMS nor grant the FDA express enforcement authority to require or implement shared REMS.

A generic drug company may, in some instances, be faced with a patent infringement claim by the RLD sponsor/plaintiff, in which the plaintiff claims that the generic drug company’s ETASU infringe the plaintiff’s patent(s). The generic drug company often will counterclaim that the alleged patent is invalid or not infringed and may allege as a counterclaim a violation of federal antitrust laws, such as the Sherman Antitrust Act. The end product is expensive litigation.

Celgene sued Barr Laboratories in 2007 for infringing numerous REMS patents for the drug Thalomid (thalidomide), for which Barr Laboratories had developed a generic equivalent; countersuits ensued.^{15,16} In this case, Celgene’s anticompetitive efforts seem to have succeeded; the 2 parties reached an agreement, and Barr Laboratories withdrew its application for the generic version of thalidomide.¹³ Of note, there has been no dispositive federal decision on whether a valid and infringed REMS patent may be used to prevent or delay the market entry of an FDA-approved generic drug.

Impact of LDNs on Patients and Healthcare Systems

Drug makers that engage in price gouging seem to follow a common business model involving LDNs. The company first identifies a sole-source drug and acquires the rights to the drug; the company then creates an LDN and subsequently raises the price. Often, the drug is an off-patent drug that has attracted little attention but is the gold standard treatment for a medical condition with few or no treatment alternatives.³ As a result of price hikes for these drugs, some patients may not be able to afford much-needed medications to treat their conditions. The [Table¹⁷⁻²³](#) lists some of the most recent and most notable examples of drugs in LDNs that were the subjects of major price increases.

LDNs may interfere with the ability of physicians, hospitals, long-term care facilities, and pharmacies to easily procure drugs and could even compromise access in emergency situations. For example, if a hospital must obtain a limited-distribution drug on a holiday or weekend, timely access is not guaranteed, and the hospital bears a considerable administrative and financial burden to order, arrange overnight shipping of, and retrieve the drug. To the extent that limited distribution interferes with the

TABLE. Examples of Drugs in Limited Distribution Networks That Have Experienced Major Price Increases

Proprietary Name (active ingredient) ¹⁷	Pharmacologic Category ¹⁸	Current License Holder ¹⁷	Year of FDA Approval ¹⁹	Current Price (average wholesale price ¹⁸ in US\$)	Price Increase
Daraprim (pyrimethamine)	Antimalarial agent	Vyera Pharmaceuticals (formerly Turing Pharmaceuticals)	1953	Thirty 25-mg tablets: \$27,000	5456%: \$13.50 to \$750 per tablet in 2015 ²⁰
H.P. Acthar Gel (corticotropin) ^{a,b}	Systemic corticosteroid	Mallinckrodt Ard Inc (formerly Questcor Pharmaceuticals, Inc)	1952 2010 (repository corticotropin)	5 mL of 80 units/mL solution: \$46,670	116,575%: \$40 per vial in 2001 to \$46,670 per vial in 2018 ²¹
Makena (hydroxy-progesterone caproate) ^a	Synthetic progestin	AMAG Pharmaceuticals	1956-1999 (proprietary name Delalutin) 2011 (Makena)	5 mL of 1.25g/5mL solution: \$2311	14,900%: \$10 to \$1500 per dose in 2011 ²²
Thiola (tiopronin) ^a	Thiol urinary tract product	Mission Pharmacal Co (formerly Retrophin)	1988	One hundred 100-mg tablets: \$3385	1900%: \$1.50 to \$30 per tablet in 2014 ²³

^aFDA-approved orphan drug.

^bIn 2001, the year that Questcor acquired H.P. Acthar Gel from Aventis Pharmaceuticals, Inc, the drug was priced at \$40 per vial. Questcor (and later Mallinckrodt) subjected the drug to a series of price increases. Its current price is over \$46,000 per vial.

ability to easily locate and obtain drugs for patients, it may actually hinder access, promote fragmentation of care, and compromise patient care.

Policy Options to Mitigate the Anticompetitive Market Impact of LDNs

There are several policy approaches to rectify the misuse of LDNs for anticompetitive purposes. We list them in descending order of their effectiveness to combat anticompetitive behavior: 1) the FDA could require the sale of drug samples to generic and biosimilar developers seeking to conduct bioequivalence testing for ANDA applications, 2) the FDA could determine which drugs can be distributed via LDNs, and 3) the FDA could mandate that drug companies disclose their intention to use LDNs.

Perhaps the most effective approach would be to authorize the FDA to require the sale of a drug product to competitors for bioequivalence testing purposes. Recognizing that the refusal of such a sale for anticompetitive purposes prolongs “lawful patent-based monopolies beyond their lawful patent life,”²⁴ the proposed Fair Access for Safe and Timely (FAST) Generics Act of 2017 (HR 2051) mandates license holders of non-REMS drugs to provide drug samples to developers within 30 days of a request at “a nondiscriminatory, commercially reasonable, market-based price for which such covered product has been previously sold by the license holder to third parties in the open market.”²⁵ The proposed Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act (S 974/HR 2212), also introduced in 2017, would enable generic or biosimilar companies to bring a civil action against the license holder if the license holder fails to give the developer access to adequate quantities of RLD, again “on commercially reasonable, market-based terms.”²⁶

The FAST Generics Act would have a greater impact than the CREATES Act because it would require the sale of samples as a condition of approval and licensing of drugs, instead of relying on expensive and time-consuming litigation. Litigation may lead some generic companies to settle with the brand manufacturer in a manner that does not further the public interest, such as withdrawal of the generic drug application or a pay-for-delay arrangement.

The statutorily granted timing of access to drug samples has the potential to influence the effectiveness of the proposed FAST Generics Act. Due to the time required for bioequivalence testing, potential patent litigation, and the approval process for generic and biosimilar drugs, access to samples for testing would ideally occur several years before a patent ends. Access to the RLD just prior to patent expiration, on the other hand, could hinder the ability of a generic or biosimilar version to come to market in a timely manner as the patent term for the brand drug expires.

In 2007, Congress gave the FDA authority to require REMS with the intent of promoting the safe use of drugs that pose known serious risks. However, the FDA currently has no authority over which drugs can be placed in LDNs. If the FDA were granted this authority, it could solicit drug makers’ rationale for seeking to apply limited distribution to a drug. We anticipate that the FDA may determine that only a subset of REMS drugs warrant limited distribution. Although this would make it more difficult for a drug company to place a drug in an LDN, it would not prohibit the use of such networks.

The least restrictive policy option is mandated disclosure by the drug manufacturer at the time drugs are placed in LDNs. Currently, the only mandatory disclosure related to restricted distribution networks is in connection with the federal 340B Drug Pricing Program, which requires the sale of covered outpatient drugs at a

discounted price to 340B-designated entities that provide safety-net care to vulnerable populations. In this case, the disclosure takes the form of “Manufacturer Notices to Covered Entities,” made public on the Health Resources and Services Administration website, which often specify changes in a drug’s distribution model to ensure that 340B purchasers have equal nondiscriminatory access to drugs that have been placed in limited or exclusive distribution networks.²⁷ For drugs in the pipeline, drug companies could be required to disclose to the FDA whether a drug will be sold in an LDN at the time of NDA or ANDA submission, and the FDA could maintain on its website a list of all drugs in LDNs. This approach does not directly impact use of LDNs; however, it fosters transparency and may be instrumental to public and private insurers in managing health plan formularies.

Finally, the FDAAA explicitly intended the use of a single REMS common to the RLD and subsequent ANDAs.^{8,14} As patent terms for REMS drugs expire and generic and biosimilar companies attempt to enter the market with competing drugs, the need for shared REMS will become more common. The CREATES Act recognizes that “clearer regulatory authority...would limit the effectiveness of bad faith negotiations over single, shared systems to delay generic approval”²⁸; the bill would allow the Secretary of HHS to require a single shared system if no comparable but distinct REMS could be developed. The FAST Generics Act offers a waiver option of the single shared REMS if good-faith negotiations between the license holder and developer do not result in an agreement.²⁵

However, both bills fail to directly address the issue of REMS patents and leave open the possibility of protracted patent infringement litigation that could continue to stymie generic and biosimilar drug development. Furthermore, the presence of multiple comparable REMS for a drug, rather than a single REMS shared by generic manufacturers and the original license holder alike, adds undue complexity and inefficiency to a system with the ultimate goal of minimizing a drug’s risk to patients regardless of the drug developer.

Misuse of LDNs to deter generic competitors may result in billions of dollars in lost savings each year, so effective legislation addressing this practice could yield tremendous financial benefits. A recent estimate calculated that the annual loss to the federal government from the misuse of REMS and restricted distribution to delay market entry of generic drugs is \$1.8 billion; private insurers lose \$2.4 billion, and consumers incur \$960 million in avoidable out-of-pocket expenses.²⁹ A Congressional Budget Office scoring of the FAST Generics Act following its introduction in the 114th Congress estimated \$2.35 billion in taxpayer savings from the bill,³⁰ whereas the CREATES Act, also introduced in the 114th Congress, was estimated to save the federal government \$3.3 billion.³¹ The CREATES Act was considered for inclusion in the 2018 federal spending bill, but despite the potential savings and bipartisan backing in Congress, CREATES was not part of the omnibus budget passed in March 2018. Yet, at least 6 of the 10 drugs projected to have

the highest pharmaceutical sales in 2022³² currently use LDNs and may continue to do so unless the laws are changed.

Conclusions

LDNs have been used inappropriately to prevent generic and biosimilar drugs from entering the market, imposing a considerable and rising cost on US payers and patients. As a means to promote market competition, the FDA could be given the authority to require the sale of drug samples to generic and biosimilar drug developers for bioequivalence testing in furtherance of the original goals of the BPCIA and the Hatch-Waxman Act. ■

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REFERENCES

1. Ellis M. Patient support services: limited distribution drugs. Presented at: CBI’s Specialty Therapies – A Forum for Payers; January 28-29, 2016; Las Vegas, NV. cbinet.com/sites/default/files/files/Ellis_Mike_pres.pdf. Accessed June 10, 2017.
2. Bolger PC. Fine-tuning specialty distribution. Pharmaceutical Commerce website. pharmaceuticalcommerce.com/business-and-finance/fine-tuning-specialty-distribution. Published June 13, 2009. Accessed June 10, 2017.
3. S Rep No. 114-429 (2016). congress.gov/congressional-report/114th-congress/senate-report/429/1.
4. Silverman E. How Martin Shkreli prevents generic versions of his pricey pill. *Pharmalot* website. pharmalot.com/how-martin-shkreli-prevents-generic-versions-of-his-pricey-pill. Published October 5, 2015. Accessed June 10, 2017.
5. *Hearings Before the US Senate Special Committee on Aging*, 114th Cong, 2nd Sess (2016) (testimony of Howard Dorfman).
6. FDA basics webinar: a brief overview of Risk Evaluation and Mitigation Strategies (REMS). FDA website. www.fda.gov/AboutFDA/Transparency/Basics/ucm325201.htm. Updated December 30, 2017. Accessed June 10, 2017.
7. Approved Risk Evaluation and Mitigation Strategies (REMS). FDA website. www.accessdata.fda.gov/scripts/cder/remis/index.cfm. Accessed March 8, 2018.
8. Federal Food, Drug, and Cosmetic Act, 21 USC §355-1(f)(8) (2007).
9. Center for Drug Evaluation and Research. Guidance for industry: bioavailability and bioequivalence studies for orally administered drug product – general considerations. FDA website. www.fda.gov/ohrms/dockets/ac/03/briefing/3995B1_07_GFI-BioAvail-BioEquiv.pdf. Published July 10, 2002. Accessed June 10, 2017.
10. Biosimilars. FDA website. www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars. Updated November 14, 2017. Accessed June 10, 2017.
11. *Examining the Impact of Voluntary Restricted Distribution Systems in the Pharmaceutical Supply Chain: Hearings Before the Subcommittee on Health Care, Benefits, and Administrative Rules of the House Committee on Oversight and Government Reform*, 115th Cong, 1st Sess (2017) (testimony of Bruce Leicher).
12. *Examining the Impact of Voluntary Restricted Distribution Systems in the Pharmaceutical Supply Chain: Hearings Before the Subcommittee on Health Care, Benefits, and Administrative Rules of the House Committee on Oversight and Government Reform*, 115th Cong, 1st Sess (2017) (testimony of Janet Woodcock, MD).
13. Sarpatwari A, Avorn J, Kesselheim AS. Using a drug-safety tool to prevent competition. *N Engl J Med*. 2014;370(16):1476-1478. doi: 10.1056/NEJMp1400488.
14. Federal Food, Drug, and Cosmetic Act, 21 USC §355-1(i)(1)(B) (2007).
15. Grande A. Celgene, Barr resolve spat over generic Thalomid. *Law360* website. www.law360.com/articles/171392/celgene-barr-resolve-spat-over-generic-thalomid. Published May 26, 2010. Accessed June 10, 2017.

16. James B. Barr strikes back at Celgene in Thalomid spat. Law360 website. law360.com/articles/37260/barr-strikes-back-at-celgene-in-thalomid-spat. Published October 11, 2007. Accessed June 10, 2017.
17. Orange Book: approved drug products with therapeutic equivalence evaluations. FDA website. www.accessdata.fda.gov/scripts/cder/ob. Updated January 2018. Accessed March 23, 2018.
18. Lexi-Drugs. Wolters Kluwer website. webstore.lexi.com/Lexi-Drugs. Accessed March 23, 2018.
19. Drugs@FDA: FDA approved drug products. FDA website. www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed March 23, 2018.
20. Pollack A. Drug goes from \$13.50 a tablet to \$750, overnight. *The New York Times*. September 20, 2015. nytimes.com/2015/09/21/business/a-huge-overnight-increase-in-a-drugs-price-raises-protests.html. Accessed June 10, 2017.
21. Wattles J. Drugmaker fined \$100M for hiking price 85,000%. CNN Money website. money.cnn.com/2017/01/18/news/drug-pricing-mallinckrodt-ftc-fine/index.html. Published January 18, 2017. Accessed June 10, 2017.
22. Stobbe M. Premature labor drug spikes from \$10 to \$1500. NBCNews.com website. nbcnews.com/id/41994697/ns/health-pregnancy/t/premature-labor-drug-spikes. Published March 9, 2011. Accessed June 10, 2017.
23. Staton T. The huge price hike as sales strategy, taken to extremes by Retrophin. FiercePharma website. fiercepharma.com/financials/huge-price-hike-as-sales-strategy-taken-to-extremes-by-retrophin. Published September 11, 2014. Accessed June 10, 2017.
24. FAST Generics Act of 2017, HR 2051, 115th Cong, 1st Sess, §2 (2017).
25. FAST Generics Act of 2017, HR 2051, 115th Cong, 1st Sess, §3 (2017).
26. CREATES Act of 2017, S 974, 115th Cong, 1st Sess, §3 (2017).
27. Manufacturer notices to covered entities. Health Resources and Services Administration website. hrsa.gov/opa/manufacturer-notices/index.html. Updated February 2018. Accessed March 8, 2018.
28. CREATES Act of 2017, S 974, 115th Cong, 1st Sess, §2 (2017).
29. Brill A. Lost prescription drug savings from use of REMS programs to delay generic market entry. Association for Accessible Medicines website. gphaonline.org/media/cms/REMS_Studyfinal_July2014.pdf. Published July 2014. Accessed June 10, 2017.
30. Welch, McKinley introduce bipartisan bill to increase consumer access, drive down costs, and boost market competition for generic pharmaceuticals [news release]. Washington, DC; US Congressman Peter Welch representing Vermont; April 7, 2017. welch.house.gov/media-center/press-releases/welch-mckinley-introduce-bipartisan-bill-increase-consumer-access-drive. Accessed September 6, 2017.
31. Leaders of Senate and House Judiciary Committees reintroduce bipartisan legislation to counter rising prescription drug prices [news release]. Washington, DC; US Senator Patrick Leahy of Vermont; April 27, 2017. leahy.senate.gov/press/leaders-of-senate-and-house-judiciary-committees-reintroduce-bipartisan-legislation-to-counter-rising-prescription-drug-prices. Accessed September 6, 2017.
32. *World Preview 2016, Outlook to 2022*. 9th ed. London, UK: EvaluatePharma; 2016. info.evaluategroup.com/rs/607-YGS-364/images/wp16.pdf.

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