vizient®

Drug Price Forecast

July-August 2018

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Introduction

It is our privilege to share with you highlights from the July 2018 Vizient® Drug Price Forecast, which offers insights into areas of interest such as specialty pharmaceuticals, oncology drugs, infectious disease agents and drug shortages. The report provides our projections of pricing behavior for the period of Jan. 1 through Dec. 31, 2019, and discusses critical issues that will likely affect the cost and use of pharmaceuticals.

The increasing expense of medications continues to invite criticism, scrutiny and calls for government intervention. Since the publication of the January 2018 edition of the Drug Price Forecast, several regulatory changes have been enacted. Some of these changes, such as increased Medicare reimbursement opportunities for biosimilars, are very positive for pharmacy providers, while others, including lower Medicare reimbursement for disproportionate share hospitals, are detrimental to the ongoing mission of improving access to high-quality care. It is important to understand the existing landscape as well as to anticipate changes that could add further complexity to pharmacy enterprises.

Executive summary

The Drug Price Forecast is our best estimate of the change in the cost of key pharmaceuticals between Jan. 1 and Dec. 31, 2019. The forecast focuses on pharmaceutical products used across multiple health-system settings, including inpatient and non-acute environments, and provides a year-over-year estimate of the expected price change.

Price change predictions for contract and noncontract product segments are shown in Table 1, along with the overall drug price inflation number for existing drugs as calculated by Vizient.

Table 1. Summary of projected drug price inflation

Product group	Estimated price change weighted by Vizient purchases (%)
Contract purchases	1.04
Noncontract purchases	3.88
Total weighted average drug price inflation estimate	4.92

Estimates based on Vizient member data.

In addition to price changes, the *American Journal of Health-System Pharmacy* advises that other factors — such as volume changes and new product introductions — must be considered when preparing a drug budget. According to a May 2018 article, volume and mix decreased 5 percent in nonfederal hospitals in calendar year 2017, but increased 4.6 percent in clinics (including both physician offices and outpatient clinics).[1] In addition, the introduction of new products accounted for 2.8 percent of expenditure growth for nonfederal hospitals and 5.3 percent of growth for clinics during the same time frame. Both sets of statistics reveal the increasing influence the expansion of non-acute care continues to have on health-system practice and expense. Table 2 shows the therapeutic classes that account for the most spend among Vizient members.

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Table 2. Summary of highest-spend therapeutic classes among Vizient members

Therapeutic category	Key products in class	Class-estimated price change (%)
Antineoplastic agents	Rituxan, Keytruda, Avastin	4.32
Disease-modifying antirheumatic agents	Remicade, Humira, Enbrel	8.57
Immunomodulatory agents	Tysabri, Copaxone, Ocrevus	7.33
Anti-infectives		1.24
Hepatitis C	Harvoni, Epclusa, Zepatier	0.00
Antibacterials/antifungals (systemic)	Daptomycin, Invanz, AmBisome	1.45
Plasma critical care		3.10
Immune globulin, intravenous (IgIV)	Gamunex, Privigen, Gammaguard	3.78
Albumin	AlbuRx, Albutein, Flexbumin	0.00
Hematopoietic agents	Neulasta, Aranesp, Procrit	2.03
Vaccines	Prevnar, Gardasil, Pneumovax	5.76

Vizient data, April 2017-March 2018.

Changes that affect pharmacy practice are a mix of positive and negative. Some favorable events have occurred recently:

- As of June 15, the Food and Drug Administration (FDA) has approved 11 biosimilars in several therapeutic classes.[2] A decision by the Centers for Medicare & Medicaid Services (CMS) to assign each biosimilar a unique reimbursement code and grant pass-through status to all biosimilars provides additional encouragement for the use of these products.[3] Most recently, the FDA commissioner has made statements on the need to remove regulatory and other barriers that can limit the uptake of these agents.[4]
- As noted in the specialty pharmacy section, integrated delivery networks are continuing to improve services by expanding clinical and operation support to provide and monitor specialty pharmaceuticals. Such efforts are critical given the continued growth of the specialty pharmaceutical pipeline and the need to demonstrate improved patient care compared with third-party specialty pharmacy providers.
- The White House has unveiled a comprehensive initiative to lower the prices of medications.[5] Although the details are still being clarified, the federal government has articulated its understanding of the need to change the dynamics that result in higher prices, which increases the likelihood that changes will be implemented.

While pharmacists and the pharmacy market continue to make substantial advances in practice, the current environment has also presented some significant challenges in the last year or so. Challenges include:

- The pharmaceutical supply chain, which continues to be fragile and subject to interruption, with the number of ongoing shortages remaining relatively static. As the market recovers from the stress of Hurricane Maria's impact on drug manufacturing facilities in Puerto Rico, Vizient continues to maintain information on the management of intravenous fluids and alternative administration strategies for many parenteral medications to help members adapt to ongoing shortages caused by that disaster.
- The opioid epidemic and some of the strategies for addressing it, which have actually exacerbated issues in the pharmaceutical supply chain. In one effort to reduce the quantity of opioids available for diversion and

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subsequent misuse, the Drug Enforcement Agency (DEA) limited the quotas of active pharmaceutical ingredients granted to pharmaceutical suppliers.[6] However, these restrictions can make it difficult to compensate for unexpected supply limitations. As a result of advocacy efforts, the DEA has now recognized the need to adjust these quotas.[7]

- Novel products that continue to be introduced at higher and higher prices. The January 2018 issue of the Drug Price Forecast noted the approval of the first chimeric antigen receptor T-cell (CAR-T) agents, tisagenlecleucel (Kymriah; Novartis) and axicabtagene ciloleucel (Yescarta; Kite Pharma/Gilead). These therapies are notable both for their novelty and for their cost: $475,000 and $373,000, respectively.[8] Those costs have since been surpassed by the introduction of voretigene neparvovec-rzyl (Luxturna; Spark Therapeutics), the first in vivo gene therapy product to treat a rare form of vision loss, whose price for treatment of both eyes is $850,000.[9]
- Reimbursement-related issues — most critically, reduced payments for disproportionate share hospitals implemented by CMS, which threaten many of our members' ability to provide care for vulnerable populations.[10] In addition, payers are increasingly focusing on the differences in cost for administering medications in different locations (e.g., physician office vs. outpatient infusion clinic).[11]

Pharmacy represents an interesting confluence of two different narratives. On the one hand, it is incredibly complicated given the regulatory issues, financial pressures, clinical requirements and forecast expectations that combine to drive practice. On the other, organizations that successfully navigate these challenges will not just succeed, but thrive. The Drug Price Forecast is intended to help relevant stakeholders anticipate and adapt to the specific and overall challenges that continue to confront health care.

Some things to keep in mind when reviewing the Drug Price Forecast:

- The forecast presents the Vizient pharmacy team's best estimate of likely drug price behavior during the identified period. However, it is important to recognize the uncertainty inherent in the projection process.
- This analysis was conducted using data from Vizient Pharmacy Program participants' purchases (price and volume) in hospital and non-acute facilities. The product mix covered by this forecast is based on participants' aggregated purchases and will differ from that of any individual facility. The products analyzed represent the top 80 percent of pharmaceutical purchases (using dollars spent on a line-item basis) made through pharmacy Authorized Distributors by Vizient Pharmacy Program participants in hospital, non-acute and pediatric settings from April 1, 2017, through March 31, 2018.
- Purchasing sterile preparations from outsourced compounders is a sizeable expense for many health systems. Our forecast does not analyze these purchases as they are not reported by our Authorized Distributors.
- Vizient bases inflation estimates for the period on price change history for the last 36 months (where available), as well as experience and current knowledge of contract allowances and marketplace factors such as expiring patents and anticipated new competition to develop an inflation estimate for each line item in the projection. The analysis does not take into account other market dynamics such as raw material scarcity and finished goods supply shortages.

Information on possible patent expirations is provided solely as a courtesy and is based on sources available at the time of publication; actual expiration dates can change because of patent challenges and litigation processes.

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There is also no guarantee that an approved generic product will be ready to enter the market at the expiration date.

A note on accuracy: Given the increasing scrutiny of drug budgets and Vizient members' expectations for greater forecast accuracy, we have begun working to review and validate our previous projections of drug prices weighted by Vizient purchases. Careful review showed that for the three editions evaluated to date, our accuracy was, on average, within 1 percent of the actual change in price (range of the difference between estimated and actual change, 0-2.5 points).

1. Schumock GT, Stubbings J, Wiest MD, et al. National trends in prescription drug expenditures and projections for 2018 [published online ahead of print May 10, 2018]. *Am J Health Syst Pharm.* 2018;75(11):e353-373.
2. FDA approved drug products. Drugs@FDA website. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed June 14, 2018.
3. CMS revises Medicare Part B biosimilar coding and payment policies. Covington & Burling LLC website. https://www.cov.com/-/media/files/corporate/publications/2017/11/cms_revises_medicare_part_b_biosimilar_coding_and_payment_policies.pdf. Published November 8, 2017. Accessed May 22, 2018.
4. Sagonowsky E. Gottlieb calls out "rigged" system that's hurting biosimilars, pledges FDA fight to boost uptake. *FiercePharma.* March 7, 2018. https://www.fiercepharma.com/pharma/fda-chief-gottlieb-calls-out-rigged-system-thats-hurting-biosim-use. Accessed May 22, 2018.
5. *American Patients First: The Trump Administration Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs.* Washington, DC: Department of Health and Human Services; May 2018. https://www.hhs.gov/sites/default/files/AmericanPatientsFirst.pdf. Accessed May 22, 2018.
6. Balick R. DEA mandates reduction in opioid manufacturing for 2018. American Pharmacists Association website. https://pharmacist.com/article/dea-mandates-reduction-opioid-manufacturing-2018. Published November 28, 2017. Accessed May 22, 2018.
7. DEA working to avoid US drug shortages [press release]. Washington, DC: US Drug Enforcement Administration; April 10, 2018. https://www.dea.gov/divisions/hq/2018/hq040918.shtml. Accessed May 22, 2018.
8. Bell J. Medicare to pay hundreds of thousands for CAR-T therapies. *BioPharma Dive.* April 6, 2018. https://www.biopharmadive.com/news/medicare-to-pay-hundreds-of-thousands-for-car-t-therapies/520806. Accessed May 22, 2018.
9. Sagonowsky E. Spark sets off gene therapy debate with $850K sticker on Luxturna. *FiercePharma.* January 3, 2018. https://www.fiercepharma.com/pharma/spark-prices-gene-therapy-luxturna-at-850k-grabbing-top-spot-pharma-s-costliest-drugs. Accessed May 22, 2018.
10. Forys A. 340B changes: what biosimilar manufacturers need to know. Center for Biosimilars website. http://www.centerforbiosimilars.com/contributor/amanda-forys/340b-changes-what-biosimilar-manufacturers-need-to-know. Published February 19, 2018. Accessed May 22, 2018.
11. Magellan Rx Management. *Medical Pharmacy Trend Report 2017.* 8th ed. https://www1.magellanrx.com/magellan-rx/publications/medical-pharmacy-trend-report.aspx. Accessed May 22, 2018.

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Timelines and approvals

New drug approvals

Drug	Indication	PDUFA date
Baricitinib	RA	Jun 30, 2018
Ivosidenib	AML	Aug 21, 2018
Eravacycline	MDR bacterial infections	Aug 28, 2018
Amikacin liposome inhalation suspension	Nontuberculosis mycobacterial lung disease	Sep 28, 2018
Doravirine	HIV	Q4 2018
Omadacycline	MDR bacterial infections	Q4 2018
Cemiplimab	Metastatic CSCC	Oct 26, 2018
Moxetumomab pasudotox	Hairy cell leukemia	Oct 31, 2018
Larotrectinib	Solid tumors	Nov 26, 2018
Baloxavir marboxil	Influenza	Dec 24, 2018
Siponimod	MS	Dec 31, 2018
Upadacitinib	RA	Dec 31, 2018
Lisocabtagene maraleucel	ALL	Dec 31, 2018
Iclaprim	MRSA	Feb 14, 2019
Ozanimod	MS	Mar 31, 2019
Risankizumab	Psoriasis	Apr 2019
Sacituzumab govitecan	Metastatic breast cancer	May 21, 2019

Abbreviations: ALL = acute lymphoblastic leukemia; AML= acute myeloid leukemia; CSCC = cutaneous squamous cell carcinoma; MDR = multi-drug resistant; MRSA = methicillin-resistant *Staphylococcus aureus;* MS = multiple sclerosis; PDUFA = Prescription Drug User Fee Act; RA = rheumatoid arthritis.

Regulatory and accreditation events

Event		Date
Comprehensive Addiction and Recovery Act 2015	Pain Management Interagency Task Force	Jul 22, 2018
FY 2019 CMS IPPS rule finalized		Aug 1, 2018
EPA Management Standards for Hazardous Waste Pharmaceuticals	Final rule in 2018	Q4 2018
DQSA Title 2: DSCSA (“track and trace”)	Drug package serialization and T3 information electronically	Nov 27, 2017 (enforcement delayed until Nov 26, 2018)
CMS MACRA	Performance measures (MIPS) enforced Jan 1, 2017	Jan 2019
USP chapter <800>	Delayed enforcement date: Jul 1, 2018	Intended official date Dec 1, 2019
USP chapter <797>	Revised Jul 27, 2018; final Jun 1, 2019	
USP chapter <795>	Revised Mar 30, 2018; final Jun 1, 2019	

Abbreviations: CMS = Centers for Medicare & Medicaid Services; DSCSA = Drug Supply Chain Security Act; DQSA = Drug Quality and Security Act; EPA = Environmental Protection Agency; FY = fiscal year; IPPS = Inpatient Prospective Payment System; MACRA = Medicare Access and CHIP Reauthorization Act; MIPS = Merit-based Incentive Payments System; USP = United States Pharmacopeia.

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Anticipated availability of new generics and biosimilars[a]

Generic name	Brand name	Earliest possible introduction
Biosimilar filgrastim (Adello)	Neupogen	Jun 15, 2018
Vardenafil	Levitra (2.5, 5, 10, 20 mg)	Q3 2018
Dalfampridine	Ampyra	Jul 2018
Ritixumab	Rituxan	Jul 2018
Cinacalcet HCl	Sensipar	Sep 8, 2018
Mometasone furoate	Asmanex Twisthaler	Sep 17, 2018
Arsenic trioxide	Trisenox	Nov 30, 2018
Silodosin	Rapaflo	Dec 2018
Mesalamine	Canasa	Dec 2018
Pimecrolimus	Elidel	Dec 26, 2018
Trastuzumab	Herceptin	Q1 2019
Lurasidone HCl	Latuda	Jan 2, 2019
Minocycline HCl	Solodyn (80 mg)	Feb 2019
Fingolimod	Gilenya	Feb 18, 2019
Ranolazine	Ranexa	Feb 27, 2019
Fosaprepitant dimeglumine	Emend (injection)	Mar 4, 2019
Fulvestrant	Faslodex	Mar 25, 2019
Solifenacin succinate	Vesicare	Apr 2019
Deferasirox tablets for oral suspension	Exjade	Apr 30, 2019
Febuxostat	Uloric	Jun 30, 2019
Itraconazole solution	Sporanox	Jun 30, 2019
Pregabalin	Lyrica (capsule)	Jun 30, 2019
Bevacizumab	Avastin	Jul 2019
Bendamustine	Treanda	Nov 30, 2019
Erlotinib	Tarceva	2019
Cyclosporine ophthalmic emulsion	Restasis	2019

[a] Projected dates of loss of exclusivity for originator drugs and generic or biosimilar entrants to the market are subject to change.

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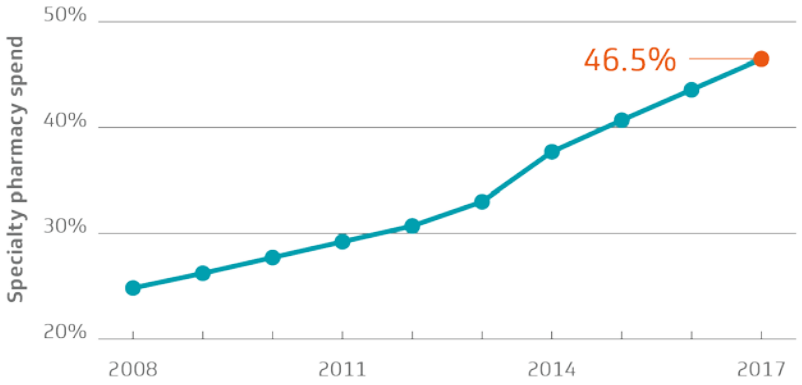
A closer look

Specialty pharmaceuticals

One of the most frequently cited points of reference to describe the expansion of the specialty pharmaceutical market has been the expected time until these medications — which are expensive but used only in small patient populations — reach 50 percent of total U.S. drug spend. The health care market continues to inch ever closer to that threshold: Recent national statistics show that the percentage of spend attributable to specialty pharmaceuticals is currently 46.5 percent (Figure 1).[1] A similar proportion is reflected in statistics examining expenditures for both the PBM industry and the management of medical benefits.[2,3] Based on the total amount of spend across care environments, the types of molecular entities approved by the FDA, and the investigational products in the development pipeline, it is certain that specialty pharmaceuticals will continue to play an increasingly important role in pharmacy budgeting.[1-3] Pharmacists, particularly those working in health-system settings, must not only be active participants in the monitoring, delivery and management of these agents, they must also be able to measure their professional contributions to improved patient outcomes.

Figure 1. Specialty pharmacy spend as a percentage of total U.S. net per capita spending



Data derived from IQVIA Institute for Human Data Science.[1]

The list of medications that account for the greatest proportion of pharmaceutical spend is still concentrated in familiar therapeutic classes such as the disease-modifying antirheumatic drugs (DMARDs), MS pharmaceuticals, agents for the treatment of hepatitis C and oncology products. These specialty classes account for large amounts of spend in both hospital and clinic settings. As a result, obtaining or developing expertise in specialty pharmaceutical management is critical to health care providers' success. It is important to focus on expanding proficiency and documenting clinical and operational results (e.g., abandonment rate, time to fill, compliance and persistence) that are superior to those of third-party specialty pharmacy providers.

More success for health-system specialty pharmacy

The January 2018 edition of the Drug Price Forecast highlighted the success of the Vanderbilt Specialty Pharmacy model within the Vanderbilt University Medical Center, which resulted in higher patient satisfaction levels, shorter time to medication initiation and increased medication adherence rates. Another academic medical center that has been successful in improving patient care via a centralized 24/7 support line for specialty pharmacy patients is the University of Utah.[4] The recently established support line is part of a comprehensive

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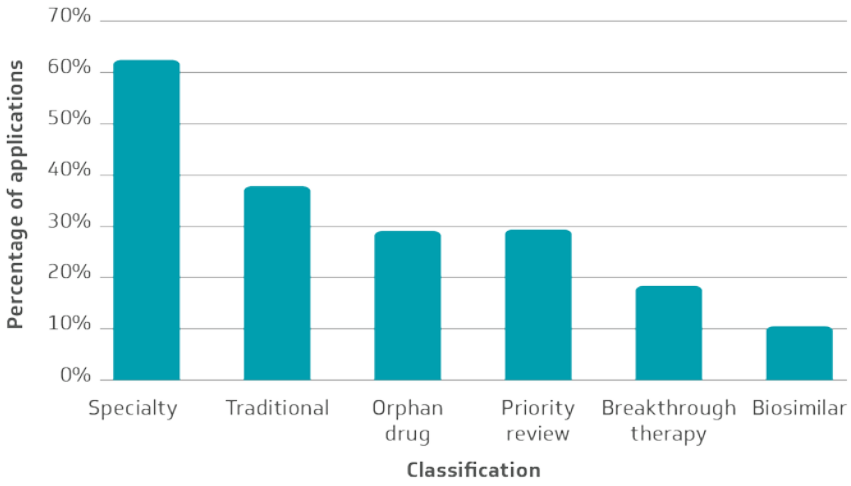
initiative to implement a pharmacy services call center that can offer improved engagement for outpatient care, encompassing nine pharmacy locations, two outpatient clinics, and the specialty pharmacy program.[4] The support line has enabled a focused and more integrated approach to meet the demands of the health system's growing specialty pharmacy service, offering a centralized way to address prior-authorization and billing questions, provide medication education and answers to clinical questions, respond to refill requests and coordinate medication delivery.[4] The support line also enables better coordination with patients' specialty clinics. The university has documented high levels of satisfaction with the new service — 95 percent of patients rated the service as excellent and 99 percent stated that a staff member was available to answer their questions "all of the time."[4] It is this level of integration and connectivity that can distinguish health-system–based pharmacy practice from other, less integrated providers.

The dynamics of specialty drug development will not change

Purchase patterns for existing medications demonstrate that specialty pharmaceuticals are driving an increasing percentage of spend in the U.S. market. That trend will not change. Figures 2 and 3 show the results of a recent analysis of the investigational drug pipeline in terms of what is known about applications presently on file with the FDA and the agents in phase 3 clinical trials.[3] In both pipelines, more than 60 percent of the products are considered specialty drugs, and many of them have additional designations such as priority review, breakthrough therapy or orphan drug status.

Figure 2. Types of drugs submitted for FDA review in 2018



Data derived from Magellan Rx Management.[3]

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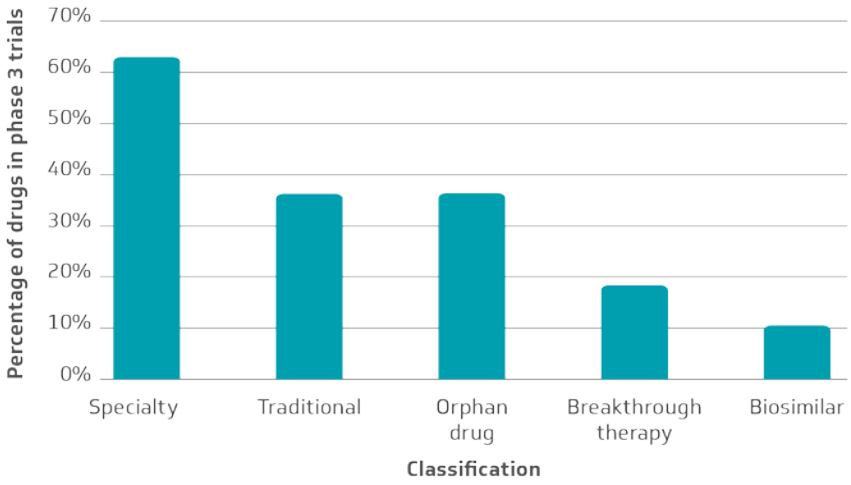
Figure 3. Types of drugs currently in phase 3 trials



Data derived from Magellan Rx Management.[3]

Conclusion

One increasingly popular concept in pharmacy practice is the "pharmacy enterprise," which reflects the reality that health-system pharmacy providers cannot view themselves solely through the lens of acute care or even a slightly expanded view that includes outpatient infusion. The realities of existing and future practice mandate competency in caring for patients in all settings. The cost of many pharmaceuticals increases the need for that competency. It is therefore critical for members to sustain their development and investment in this area.

1. IQVIA Institute for Human Data Science. *Medicine Use and Spending in the U.S.: a Review of 2017 and Outlook to 2022.* https://www.iqvia.com/institute/reports/medicine-use-and-spending-in-the-us-review-of-2017-outlook-to-2022. Published April 19, 2018. Accessed June 3, 2018.
2. Express Scripts. *Drug Trend Report 2017.* St Louis, MO: Express Scripts; February 2018. http://lab.express-scripts.com/lab/drug-trend-report/2017-dtr. Accessed June 3, 2018.
3. Magellan Rx Management. *Medical Pharmacy Trend Report 2017.* 8th ed. https://www1.magellanrx.com/magellan-rx/publications/medical-pharmacy-trend-report.aspx. Accessed May 22, 2018.
4. Rim MH, Thomas KC, Chandramouli J, Barras SA, Nickman NA. Implementation and quality assessment of a pharmacy services call center for outpatient pharmacies and specialty pharmacy services in an academic health system. *Am J Health-Syst Pharm*. 2018;75(10):633-641.

Pediatrics

Recent approvals

Approvals of specialty drugs for pediatric diseases, gene therapy and CAR-T treatments have dominated the headlines in the last year. One of the most significant events was the FDA approval in November 2017 of emicizumab-kxwh (Hemlibra; Genentech), a humanized monoclonal antibody indicated to prevent or reduce frequency of bleeding episodes in patients with hemophilia A who have developed antibodies or inhibitors. In April 2018, under breakthrough therapy designation, it was approved for all hemophilia A patients regardless of inhibitor presence.[1]

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In February 2018, the FDA approved a treatment for cystic fibrosis in patients with two mutations of F508del, tezacaftor/ivacaftor (Symdeko; Vertex Pharmaceuticals), which added another option for patients who do not tolerate lumaftor/ivacaftor (Orkambi; Vertex Pharmaceuticals).

Benralizumab (Fasenra; AstraZeneca) was approved in November 2017 for the treatment of pediatric asthma; the agent is an anti-eosinophil monoclonal antibody targeting the interleukin-5 receptor. In phase 3 trials, benralizumab was shown to reduce corticosteroid doses by 75 percent and overall exacerbation rates by 70 percent.[2]

In April 2018, the FDA advisory panel unanimously recommended the approval of an epilepsy medication, cannabidiol (Epidiolex; GW Pharmaceuticals), on the basis of improvements in quality of life and seizure frequency in patients with refractory epilepsy, including Lennox-Gastaut and Dravet syndromes.[3] Approval was granted in June but the classification schedule has not yet been determined; the classification decision will have an impact that reaches well beyond this single product.

Cost increases driven by specialty drugs, outpatient care

Pharmaceutical costs are continuing to climb in the pediatric sector due to the targeting of specialty disease, as well as a large increase in outpatient spend driven by the substantial shift in care to this setting.

The cost of CAR-T and gene therapy, such as tisagenlecleucel (Kymriah) and voretigene neparvovec-rzyl (Luxturna), remains a consideration for pediatric care centers.[4] Kymriah is the first of many in the pipeline targeting individualized immunocellular therapy. A single infusion of Kymriah is $475,000.[5] Luxturna, endorsed by the FDA in October 2017, is a gene replacement therapy for RPE65-medicated inherited retinal dystrophy, which can cause complete blindness.[6,7] Its cost for the treatment of both eyes totals $850,000. These novel therapies present new financial challenges for hospitals. Institutions must review their procurement and administration policies, since these drugs have significant restrictions on handling, storage and administration. In the case of Kymriah, the therapy can only be administered at preapproved centers and patients must be able to reach the center within two hours for at least four weeks after administration in case of emergency.

In the pipeline

The investigational pipeline in pediatrics continues to focus on treatment of targeted diseases using monoclonal antibodies, gene therapy and orphan drugs. A gene therapy for the treatment of Duchenne muscular dystrophy, a genetic degenerative disease that leads to progressive weakness of muscles, is currently undergoing a phase 2a safety trial. The goal of this therapy is to replace the affected mRNA with mutations between exons 18 and 58.[8] Another gene therapy under investigation to treat type 1 spinal muscular atrophy is AVXS-101 (AveXis), intended to be an intravenous alternative to intrathecal nusinersen (Spinraza). An open-label, single-arm, single-dose, multicenter trial, known as STR1VE, is being conducted to evaluate the efficacy and safety of a one-time intravenous infusion of AVXS-101.[9]

Table 3 lists additional products in development that, in some cases, are expected to have substantial costs associated with their use.

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Table 3. Important late-phase investigational drugs with pediatric studies ongoing

Disease state/condition	Drug	Clinical trial phase	Manufacturer
Peanut allergy	AR101	3	Aimmune
Cutaneous T-cell lymphoma	SGX301 (bronchitol)	3	BioTherapeutics
Cystic fibrosis	Inhaled mannitol	3	Pharmaxis
Dravet syndrome	Fenfluramine (ZX008)	3	Zogenix
Progressive familial intrahepatic cholestasis	A4250	3	Albireo Pharma
	Maralixibat (SHP625)	3	Shire
Relapsing-remitting multiple sclerosis	BG00012	3	Biogen
Spinal muscular atrophy	LM1070	2	Novartis
	RG7916	2	Roche/Genentech/PTC Therapeutics/ Spinal Muscular Atrophy Foundation
	CK-2127107	2	Cytokinetics/Astellas Pharma

Data derived from ClinicalTrials.gov, Cure SMA, Cystic Fibrosis Foundation.[9-12]

1. Hemlibra (emicizumab-kxwh) [package insert]. South San Francisco, CA; Genentech, Inc. November 2017.
2. Nair P, Wenzel S, Rabe KF, et al; ZONDA Trial Investigators. Oral glucocorticoid-sparing effect of benralizumab in severe asthma. *N Engl J Med.* 2017;376(25):2448-2458.
3. GW Pharmaceuticals announces the unanimous positive result of FDA advisory committee meeting for the first plant-based pharmaceutical cannabidiol treatment for seizures in patients with two rare, severe forms of epilepsy [press release]. Carlsbad, CA: GW Pharmaceuticals; April 18,2018.
4. FDA approval brings first gene therapy to the United States [press release]. Silver Spring, MD: Food and Drug Administration; August 30, 2017. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm574058.htm. Accessed June 4, 2018.
5. Hagen T. Novartis sets a price of $475,000 for CAR T-cell therapy. *OncLive.* August 30, 2017. http://www.onclive.com/web-exclusives/novartis-sets-a-price-of-475000-for-car-tcell-therapy. Accessed June 4, 2018.
6. Stein R. FDA panel endorses gene therapy for a form of childhood blindness. *National Public Radio.* October 12, 2017. https://www.npr.org/sections/health-shots/2017/10/12/557183740/fda-panel-endorses-gene-therapy-for-a-form-of-childhood-blindness. Accessed June 4, 2018.
7. Russell S, Bennett J, Wellman JA, et al. Efficacy and safety of voretigene nepavovec (AAV2-hRPE65v2) in patients with RPE65-medicated inherited retinal dystrophy: a randomized, controlled, open-label, phase 3 trial. *Lancet.* 2017;390(10097):849-860.
8. The first SMA gene therapy in human trials. AveXis website. https://avexis.com/research-and-development. Accessed June 4, 2018.
9. A study to investigate the efficacy and safety of ZX008 (fenfluramine HCL) as an adjunctive therapy in children and adults with Lennox-Gastaut syndrome. ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT03355209. Published November 28, 2017. Updated June 4, 2018. Accessed June 8, 2018.
10. Duchenne muscular dystrophy clinical trials. ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/results?cond=Duchenne+Muscular+Dystrophy&term=&cntry=&state=&city=&dist=. Accessed June 8, 2018.
11. SMA Drug Pipeline. Cure SMA website. http://www.curesma.org/research/our-strategy/clinical-trials. Accessed June 15, 2018.
12. Drug development pipeline. Cystic Fibrosis Foundation website. https://www.cff.org/trials/pipeline. Accessed June 2, 2018.

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Key therapeutic class summaries

Oncology

A closer look

The number of oncology drugs with price tags above $100,000 is increasing at an unsustainable rate. In response, various stakeholders have begun discussing ways to move from a volume- to a value-based approach to product costs and increasing the transparency of treatment expenses.

- Novartis initiated an outcomes-based contract with CMS to receive payment on tisagenlecleucel (Kymriah) only if the patient responds after the first month of treatment.
- CMS initiated a national coverage analysis for CAR-T therapies to determine whether Medicare will reimburse for these types of therapies; the analysis is expected to be completed by May 17, 2019.
- CMS also introduced an improved Drug Dashboard that includes year-over-year drug pricing and manufacturer price increases.

Health care reform has also had a significant impact on oncology care by creating programs to measure quality and implementing policies that will affect how oncology treatments are administered.

- In February, the Oncology Care Model developed by the Center for Medicare & Medicaid Innovation published its first annual report evaluating data for the baseline period.
- The “right-to-try” bill was signed into law on May 30. This controversial piece of legislation is in direct conflict with the FDA’s compassionate use program and the effects of the new enactment remain to be seen.
- Merit-based Incentive Payment System (MIPS) cost performance for 2018 increased to a 10 percent weighted performance period from zero. An increase up to 30 percent cost weight will start with the 2019 MIPS performance period.

What’s ahead

Additional indications for current PD-1 and PD-L1 products are expected to be approved by the FDA by the end of 2018, as is a new product in this category. Utilization of immunotherapy is expected to continue to grow as the number of indicated disease states increases and its role in therapy widens.

Innovative agents to watch for include:

- Moxetumomab pasudotox, an anti-CD22 recombinant immunotoxin indicated for treatment of hairy cell leukemia
- Larotrectinib, a tropomyosin receptor kinase (Trk) inhibitor for solid tumors
- Ivosidenib, for the treatment of acute myeloid leukemia in patients with IDH-1 mutations and also for solid tumors

Three biosimilar products are to be reviewed this year by the FDA. However, patent litigation between the various drug manufacturers and reference drug suppliers will continue to block launch of the new products.

- Filgrastim (Adello): Approval expected in third quarter of 2018
- Filgrastim (Hospira): Approval expected in third quarter of 2018
- Pegfilgrastim (Coherus): Approval expected in fourth quarter of 2018

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New generics expected within the next year include:

- Arsenic trioxide (Trisenox): Expected to launch by fourth quarter of 2018
- Abiraterone acetate 250 mg tablets (Zytiga): Possible launch in first half of 2019

Drug manufacturers will continue to reformulate original patented products such as Rituxan Hycela (rituximab/hyaluronidase human) and come to market with novel drug formulations like Vyxeos (daunorubicin/cytarabine) that may have a significant impact on outpatient chemotherapy infusion clinics' budgets and administration times.

Infectious disease agents

Systemic antibacterials and antifungals

What's ahead

The anti-infective pipeline (Table 4) is robust as a result of regulatory actions such as protections granted through the Generating Antibiotics Incentives Now (GAIN) Act, which offers an additional five years of patent protection for antibiotics that treat serious or life-threatening infections,[1] and the 21st Century Cures Act, which provides a unique mechanism for the FDA to review and approve new antibiotics specifically for use in patients with unmet medical needs.[2]

Table 4. Selected antibacterials expected to be submitted to the FDA for approval by mid-2019[a]

Investigational drug name	Manufacturer	Class	Proposed indication(s)	Status[b]
Cefiderocol	Shinogi	Siderophore-cephalosporin	cUTI, HABP/VABP, CRE	Phase 3
Eravacycline	Tetraphase	Tetracycline	cIAI (failed cUTI study)	PDUFA date Aug 28, 2018
Fosfomycin (intravenous)	Zavante	Phosphonic acid derivative	cUTI, cIAI, HABP/VABP, ABSSSI	Phase 3
Iclaprim	Motif Bio PLC	Dihydrofolate reductase inhibitor	ABSSSI, HABP	NDA filed Q2 2018
Lefamulin	Nabriva	Pleuromutilins	CABP, ABSSSI	Estimated NDA filing Q4 2018
Omadacycline	Paratek	Tetracycline	CABP, ABSSSI	NDA filed Q2 2018 (PDUFA estimated Oct 2018)
Plazomicin	Achaogen Inc.	Aminoglycoside	cUTI	Approved Jun 25, 2018
Imipenem-cilastatin/relebactam	Merck	Carbapenem	cUTI, AP, HABP/VABP	Phase 3

[a] Adapted from Pew Charitable Trusts.[3]

[b] Status may vary by proposed indication. The data in this column reflects the latest trial information and current FDA status for the indication(s) most likely to be included in the initial FDA approval.

Abbreviations: ABSSSI = acute bacterial skin and skin structure infection, AP = acute pyelonephritis, CABP = community-acquired bacterial pneumonia, cIAI = complicated intra-abdominal infection, CRE = carbapenem-resistant *Enterobacteriaceae,* cUTI = complicated urinary tract infection, HABP = hospital-acquired bacterial pneumonia, NDA = new drug application; PDUFA = Prescription Drug User Fee Act, VABP = ventilator-associated bacterial pneumonia,

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Investigational antifungals currently in development are either broad spectrum or are formulated for oral absorption. The recent emergence in the U.S. of *Candida auris*, a multi–drug-resistant fungus that is difficult to treat,[4] emphasizes the need for new antifungal therapies.

There is an increased focus on identifying innovative ways to treat infectious diseases by augmenting the patient's innate immunity to fight infection. Monoclonal antibodies similar to bezlotoxumab (Zinplava; Merck), which was approved in 2016 for the adjunctive treatment of infections caused by *Clostridium difficile* (now known as *Clostridioides difficile*), are in development. And extensive research on the human microbiome and its impact on the development of infection is being conducted, including therapies that utilize biologic material from donors (e.g., stool) as a preventative therapy to reduce the recurrence of *C. difficile* infection.

1. Department of Health and Human Services. Generating Antibiotic Incentives Now. Food and Drug Administration website. https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM595188.pdf. Accessed May 22, 2018.
2. Tracking the global pipeline of antibiotics in development: issue brief. The Pew Charitable Trusts website. http://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2014/03/12/tracking-the-pipeline-of-antibiotics-in-development. Published March 12, 2014. Accessed May 22, 2018.
3. Antibiotics currently in global clinical development. The Pew Charitable Trusts website. http://www.pewtrusts.org/~/media/assets/2018/03/antibiotics_clinical_dev_table_february2018.pdf?la=en. Updated December 2017. Accessed May 22, 2018.
4. *Candida auris.* Centers for Disease Control and Prevention website. https://www.cdc.gov/fungal/candida-auris/index.html. Updated May 18, 2018. Accessed May 23, 2018.

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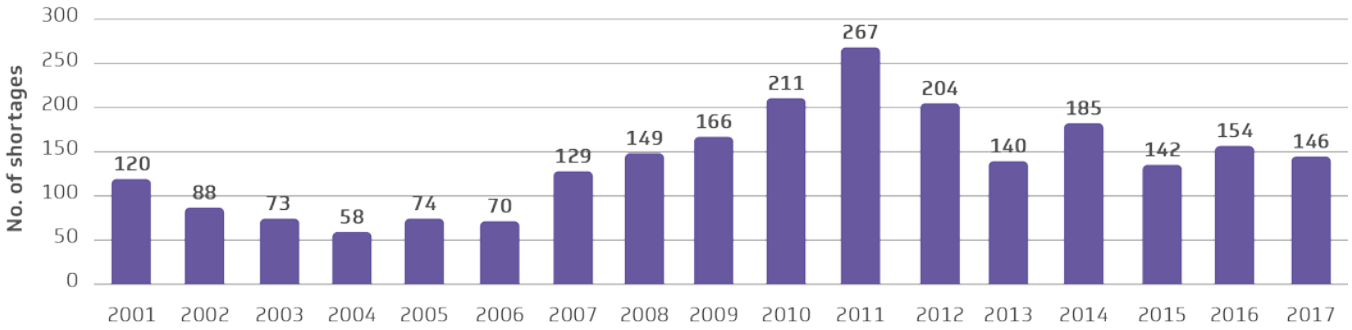
Hot topics

Drug shortages: Continuing the fight

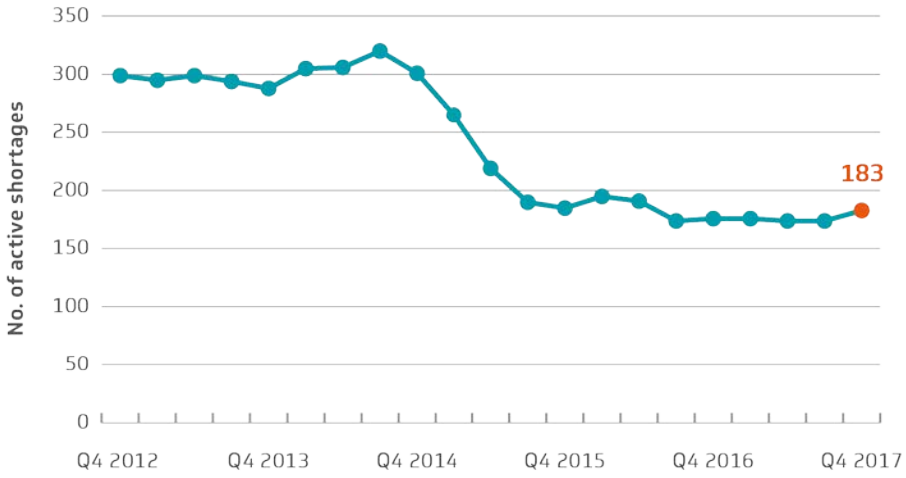
The U.S. pharmaceutical industry is an interesting study in contrasts. On the one hand, we have witnessed a period of incredible innovation in terms of recombinant technologies, immunotherapies, and now even the first gene therapy product, that hold the promise for not just mitigation of illness, but resolution of disease states. With this advancement, however, have come ever-increasing prices. And at the same time, we remain locked in a battle — now going on for nearly two decades — with a generic supply chain whose only consistent attribute is continual interruptions of supply (Figures 4 and 5), and the expenses associated with managing these interruptions.

Figure 4. Number of drug shortages in the U.S., by year



Data derived from University of Utah Drug Information Service.[1]

Figure 5. Total number of active shortages, 2012-2017



Data derived from University of Utah Drug Information Service.[1]

The collision of health care crises

So far, 2018 has been marked by drug shortages that have been made worse by actions aimed at addressing another public health crisis. The steps taken by the DEA to limit quotas of opioid active pharmaceutical

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ingredients were, of course, intended to have the positive outcome of limiting opportunities for diversion.[2] But when a major injectable supplier had to leave the market temporarily to address manufacturing issues, there was no process to redistribute that supplier's allocation of ingredients to other companies that could make up for the lost capacity. Fortunately, the DEA responded to requests from Vizient and other organizations to alter the allocated quotas,[3] but given the timeline required for manufacture, changes in allocation cannot immediately rectify supply constraints. The policy change should, however, at least prohibit quota limitations from exacerbating current shortages.

How do we respond?

Step 1: Communication

What the last two decades have taught us is that accurate and timely communication of actionable information is critical to successfully mitigating drug shortages. Most organizations instituted and refined practices to promote such communication and to educate pharmacists, physicians and nurses about practice changes necessitated by shortages. We at Vizient have long supported this commitment to education and have helped meet members' needs for information and education with the help of the drug information team at University of Utah Health. The organization is a long-time Vizient member and its drug information team is nationally recognized for its work on drug shortage monitoring and mitigation strategies.

Another area where the Utah team has provided leadership is increasing awareness of the impact of drug shortages through the published literature. University of Utah Health's Senior Director Erin Fox, PharmD, has been a contributing author to four recent articles describing the historical effects of drug shortages on the supply of adult critical care medications, neuroleptic therapies, vaccines and immune globulins, and agents used in ambulatory pediatric populations.[4-7]

Effective communication remains a critical element to addressing drug shortages and is one that Vizient endorses and will continue to support.

Step 2: Advocacy

The DEA's response to the requests from Vizient and other organizations to modify quotas of opioid ingredients was welcome. The success of this advocacy initiative suggests that Vizient and its members must continue their work in this area. As noted in the 2018 Vizient Pharmacy Charter, supporting a stable and reliable supply of high-quality medications is a strategic imperative for our members and something we must achieve if we hope to move beyond the limitations we currently experience.

Step 3: Strengthening supply

Another strategy that Vizient has employed to minimize the impact of shortages on our members and the patients they serve is the Novaplus® private-label program. Although it cannot eradicate drug shortages, the Novaplus portfolio has been successful in easing their effects on Vizient members. For example, we recently reviewed the American Society of Health-System Pharmacists drug shortage list[8] (created by the University of Utah) to identify supply limitations for medications primarily used in the health-system setting, and then examined fill rates across our membership for these molecules. For many of the drugs for which national shortages have been identified, Vizient members had fill rates greater than 75 percent (unpublished data).

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With the ideal of eradicating drug shortages in mind, we at Vizient are looking at additional approaches to sourcing activities involving Novaplus as a way to collaborate with suppliers to create a more stable supply.

Conclusion

Beyond understanding the impact and causes of drug shortages, we must implement meaningful changes to reduce their number and length and mitigate their effects. Education has been a cornerstone of our strategies and will retain its importance, as will amplifying the voice of our members through advocacy initiatives. Additional areas for innovation, including the expansion of successful tools such as the Novaplus program, are being actively investigated.

1. University of Utah Drug Information Service. Drug shortages statistics. American Society of Health-System Pharmacists website. https://www.ashp.org/Drug-Shortages/Shortage-Resources/Drug-Shortages-Statistics. Accessed June 14, 2018.
2. Balick R. DEA mandates reduction in opioid manufacturing for 2018. American Pharmacists Association website. https://pharmacist.com/article/dea-mandates-reduction-opioid-manufacturing-2018. Published November 28, 2017. Accessed May 22, 2018.
3. DEA working to avoid US drug shortages [press release]. Washington, DC: US Drug Enforcement Administration; April 10, 2018. https://www.dea.gov/divisions/hq/2018/hq040918.shtml. Accessed May 22, 2018.
4. Mazer-Amirshahi M, Goyal M, Umar SA, et al. U.S. drug shortages for medications used in adult critical care (2001-2016). *J Crit Care.* October 2017;41:283-238. doi:10.1016/j.jcrc.2017.06.005.
5. Omorodion JO, Algahtani RM, Zocchi MS, Fox ER, Pines JM, Kaminski HJ. Shortage of generic neurologic therapeutics: an escalating threat to patient care. *Neurology.* 2017;89(24):2431-2437.
6. Ziesenitz VC, Mazer-Amirshahi, Zocchi MS, Fox ER, May LS. US vaccine and immune globulin product shortages, 2001-2015. *Am J Health Syst Pharm.* 2017;74(22):1879-1886.
7. Donnelly KA, Zocchi MS, Katy TA, Fox ER, van den Anker JN, Mazer-Amirshahi ME. Prescription drug shortages: implications for ambulatory pediatrics [published online ahead of print May 8, 2018]. *J Pediatr.* doi:10.1016/j.jpeds.2018.04.008.
8. Current drug shortages. American Society of Health-System Pharmacists website. https://www.ashp.org/Drug-Shortages/Current-Shortages. Accessed May 23, 2018.
9. Abelson R, Thomas K. Fed up with drug companies, hospitals decide to start their own. *New York Times.* January 18, 2018. https://www.nytimes.com/2018/01/18/health/drug-prices-hospitals.html. Accessed May 23, 2018.

Next DSCSA milestone: November 2018

The Drug Quality and Security Act Title II: Drug Supply Chain Security Act (DSCSA) was signed into law in November 2013. The DSCSA establishes a national system to identify and trace certain prescription drugs as they are distributed in the U.S. and preempts existing state pedigree requirements. It also outlines a 10-year plan of the critical steps in building an electronic, interoperable system that will facilitate the exchange of information at the individual package level about where a drug has been in the supply chain (Table 18).

Table 18. DSCSA timeline: important upcoming dates[a]

2019	2020	2023
Nov 27 **Distributor:** • Receive product with unique identifiers • Accept returns only with TI, TS	**Nov 27** **Dispenser:** • Accept only serialized products (2D barcode identifiers) • Verification of unique product identifiers	**Nov 27** **Manufacturer:** • Participate in package level traceability system **Distributor:** • Participate in package level traceability system **Dispenser:** • Participate in package level traceability system

[a] Data derived from DSCSA implementation plan.[1]

Abbreviations: FDA = Food and Drug Administration; TH = transaction history; TI = transaction information; TS = transaction statement.

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By 2023, DSCSA will enable verification of the legitimacy of the drug product identifier down to the package level, enhance detection and notification of illegitimate products in the drug supply chain, and facilitate more efficient recalls of drug products. The first milestones for dispensers (i.e., pharmacies) were the requirement to quarantine and investigate suspect product and to be able to retain transaction data.

The Office of the Inspector General (OIG), an organization within the U.S. Department of Health and Human Services that is tasked with ensuring the integrity of U.S. health care programs, oversees the DSCSA initiative. In late 2016, the OIG began a review to assess dispenser knowledge of DSCSA and compliance with the program, conducting hour-long interviews with 40 dispensers focused on product transaction documentation, trading partner verification and any best practices identified. A March 2018 report of the study[2] stated that the OIG found varying degrees of compliance with the DSCSA dispenser responsibilities; some dispensers lacked awareness of all requirements and some were missing transaction information. As a result of their review, the OIG recommended that the FDA provide educational outreach to dispensers, specifically on the need to ensure receipt of complete drug product tracking information from trading partners before taking ownership of products. To comply with the OIG recommendation, the FDA offered a series of free continuing education webinars.

The next major milestones for dispensers are accepting only serialized products (effective Nov. 27, 2020) and participating in the package-level traceability system along with all trading partners (effective Nov. 27, 2023). But serialized products have already entered the supply chain, so pharmacies need to be aware of how the milestone for manufacturers, which takes effect this November, will affect them. The serialization milestone, whose enforcement date was delayed until Nov. 26, 2018, requires manufacturers and repackagers to place a unique product identifier on each package and homogeneous case. This identifier, which must be included as a 2D barcode in addition to the current human-readable format, contains the following:

- GTIN (Global Trade Item Number) — a 14-digit identifier that contains the encoded 10-digit NDC
- Serial number of up to 20 characters
- Lot number of up to 20 characters
- Expiration date in a six-digit format (YYMMDD)

The information contained in the unique product identifier enables the product to be tracked back through the supply chain by a human or a computer. This feature, along with the Nov. 27, 2017, requirement for manufacturers to provide transaction data in an electronic format, brings the system one step closer to interoperability.

Pharmacies should be aware that they will soon see changes in drug packaging due to the serialization requirement. In addition, it is important that dispensers have barcode scanners that can read the new serialized 2D barcodes at product receipt, when storing medications in automated dispensing cabinets and before medication administration. The pharmacy informatics team can provide critical support for the next DSCSA steps. Pharmacies should also consult with their wholesalers about how the new and evolving requirements of DSCSA will be communicated to them.

1. Drug Supply Chain Security Act (DSCSA) implementation plan. Food and Drug Administration website. https://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/ucm382022.htm. Updated March 1, 2017. Accessed June 19, 2018.
2. *Drug Supply Chain Security: Dispensers Received Most Tracing Information* (OEI-05-16-00550). Washington, DC: Department of Health and Human Services Office of Inspector General; March 2018. https://oig.hhs.gov/oei/reports/oei-05-16-00550.pdf. Accessed June 15, 2018.

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