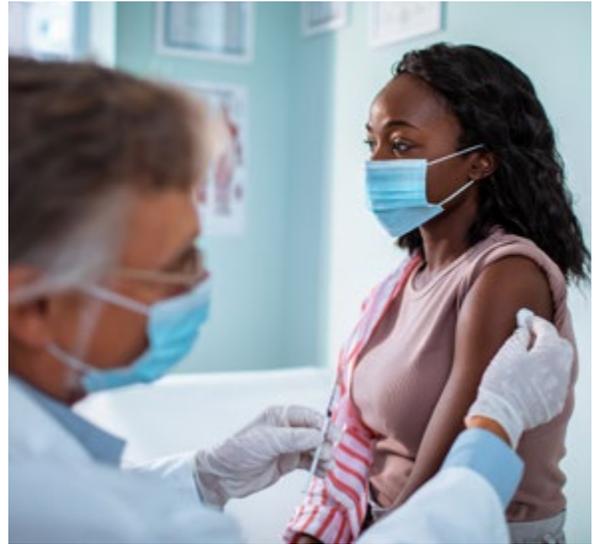


Pharmacy Market Outlook

Keeping you at the forefront of drug price
projections and market developments

Winter 2021



Outlook preparation, process and assumptions

Some things to keep in mind when reviewing the Pharmacy Market Outlook (formerly the Drug Price Forecast):

- This report 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.
- The 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 outlook is based on participants' aggregated purchases and will differ from that of any individual facility. To help you assess your own data using the information in this report, figures are presented using generic names and therapeutic categories. The Vizient Drug Budget Forecast Report, located in the Vizient Savings Actualyzer™ — Pharmacy platform, is designed to help you capture your institution's detailed pharmacy purchases. Contact us at pharmacyquestions@vizientinc.com if you have questions about accessing the report.
- The products analyzed comprise the top 85% of pharmaceutical purchases (using dollars spent on a line-item basis) made through pharmacy Authorized Distributors by Vizient Pharmacy Program participants in hospital, nonacute, and pediatric settings from October 1, 2019, through September 30, 2020. Purchases made through the 340B program were excluded from the analysis. The analysis also does not include direct purchases.
- Purchasing sterile preparations from outsourced compounders is a sizeable expense for many health systems. This report does not analyze these purchases as they are not reported by our Authorized Distributors. If your facility uses outsourced compounding services, remember to factor those purchases into your budget. Vizient has noted regular price increases from our contracted suppliers in this area and we believe that this trend will continue.
- Vizient uses price change history for the last 36 months (where available), as well as experience and knowledge of current 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 given the present difficulty in obtaining this information. However, Vizient continues to advocate for greater transparency throughout the supply chain for all components that contribute to finished dosage forms.
- 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. There is also no guarantee that an approved generic or biosimilar product will be ready to enter the market by the expiration date. Manufacturers also may file a request for exclusive marketing rights with the US Food & Drug Administration (FDA) for periods ranging from 180 days to 7 years depending on the category. If granted, this period of exclusivity may or may not be synchronized with the patent status and can further delay the introduction of competition into the market.
- Information about new drugs in the pipeline is available by contacting pharmacyquestions@vizientinc.com. Cost information is not usually available for new products until they receive FDA authorization or approval; however, health care organizations should review the literature on any new agent to determine its place in therapy for their specific patient populations and to develop guidelines for cost-effective use of new, expensive drugs.

Disclaimer: This document is a projection of price behavior only. It is necessary to consider changes in volume and mix as well as the introduction and adoption of new drugs and other factors when preparing your drug expenditure budget.

This document is compiled based on information gathered from many primary and secondary sources, which Vizient believes to be accurate to the best of its knowledge at the time of publication. It is intended as general information only and is provided as an accommodation to members. Use of this data is at your sole risk. This information is presented "as is" and without any warranty or guarantee, expressed or implied, as to completeness or accuracy, or otherwise.

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Letter from our group senior vice president, pharmacy solutions



Dan Kistner, PharmD

Group Senior Vice President,
Pharmacy Solutions
Vizient

Welcome to the Winter 2021 issue of the newly renamed Vizient® Pharmacy Market Outlook (formerly the Drug Price Forecast). Although drug pricing behavior is still and will remain an essential component of this offering, the new name better reflects its broad, strategic scope. Our aim, as always, is to provide a comprehensive review of the trends and dynamics affecting pharmacy practice, taking advantage of the expertise and experience of the Vizient Center for Pharmacy Practice Excellence.

In this issue, we examine the outlook for health care and pharmacy practice beyond the shadow of COVID-19. At this time last year — on January 30, 2020 — the World Health Organization declared the novel coronavirus (SARS-CoV-2) outbreak to be a public health emergency of international concern, its highest alert level. It sometimes seems impossible to believe that 12 months have passed since the onset of the COVID-19 pandemic. At the same time, however, the enormity of the crisis makes it feel like we have endured many decades' worth of human suffering compressed into a single year.

Similarly, the COVID-19 outbreak has given us divergent perceptions of the health care environment. On the one hand, the pandemic has demanded our attention to the exclusion of almost every other priority. At the same time, it has illuminated the lingering weaknesses in the US health care system and how they limit our capacity to respond to new challenges effectively. The many problems we have experienced during the outbreak — shortages of personal protective equipment and essential drugs, difficulty identifying new treatment pathways and disseminating information rapidly and accurately, complicated drug development systems, absence of robust population health management strategies, and perhaps of greatest concern, limited access to care for vulnerable patients — predate COVID-19, but their continuing presence has amplified the virus' ability to do harm.

The Pharmacy Market Outlook provides insights from our experts on the next 6 to 18 months of pharmacy practice from a variety of perspectives: drug pricing, medication use, regulatory, drug development pipeline output, sourcing goals, and advocacy. It also offers information on critical services we provide, including [strategies to optimize the delivery and administration of COVID-19 vaccines](#) and our [Novaplus® Enhanced Supply Program](#), which to date has secured a US-based inventory of 53 million additional units of essential medications for participating members.

As the long-awaited COVID-19 vaccines become available, we can begin to imagine a more normal existence for the health care industry and the wider community. However, even the introduction of vaccines does not mean we are at the end of this battle. The delivery of vaccines to all those needing (and wanting) immunization is one of the most complicated public health endeavors ever attempted and will require coordination among all elements of the health care system. Furthermore, even after the virus is no longer a widespread threat, we cannot revert to an environment in which clinicians, no longer burdened by the intensity of COVID-19 management, must continue to compensate for systemic deficiencies. Instead, clinicians, including pharmacists, must construct a health care delivery mechanism that is resilient and flexible enough to respond rapidly to new crises, disseminate and adopt best practices quickly, and consistently give patients access to high-quality treatments and the best possible outcomes.

That's why we are here. We at Vizient have been honored to work alongside you during the depths of the COVID-19 crisis, and we remain committed to supporting your continued recovery, increasing the resilience of the supply chain, and charting a new path for pharmacy leadership in an increasingly complicated clinical practice setting. That commitment includes offering you the expertise, services, and analytics you need to set pharmacy practice on a path of continuous innovation and better patient outcomes. As the events of 2020 showed, we cannot foresee every challenge we will face. However, the strength of our members and the connections we have established enable us all to be prepared for changes as they occur.

Given the global scale of the COVID-19 crisis, it seems appropriate to consider it in the context of other major worldwide events. In 1942, after many months of setbacks and losses during World War II, the Allies won a decisive victory over the Axis powers at the Second Battle of El-Alamein. Not only did this success halt the progression of the Axis powers, it greatly lifted the morale of the Allies. During a speech after this battle, British Prime Minister Winston Churchill reflected, "Now this is not the end. It is not even the beginning of the end, but it is, perhaps, the end of the beginning."¹ It is my sincere hope that by the time I write the January 2022 version of this letter, we will be not at "the end of the beginning," but at the true end of the COVID-19 crisis — and within sight of the end of the many other obstacles that have hindered our collective goal of ensuring better health care for the US and the world. I eagerly look forward to that day.

Thank you for your membership in Vizient and your partnership in improving the quality and value of health care through pharmacy leadership. Your efforts and your willingness to put yourselves in harm's way in this most trying time have been vital to your patients and our nation. We are honored to work with and support you as we move out of the shadow of this global crisis.

A handwritten signature in black ink, appearing to read "David Kristman". The signature is fluid and cursive, with a large, stylized initial "D".

¹ The end of the beginning. Speech by Winston Churchill at The Lord Mayor's Luncheon, Mansion House, November 10, 1942. The Churchill Society. Accessed November 9, 2020. <http://www.churchill-society-london.org.uk/EndoBegn.html>

Projected timelines and approvals

● New drug approvals ● Regulatory and accreditation events ● Anticipated availability of new generics and biosimilars*

EPA amendment to the P075 listing for nicotine

FDA-approved, over-the-counter nicotine replacement therapies (i.e., nicotine patches, gums and lozenges) are no longer considered acute or even hazardous waste when discarded.

Aug 21, 2019, in Iowa, Alaska, Indian Country, and US territories (except Guam); other states have the option to adopt the amendment

USP General Chapter <825>

Describes best practice and quality standards for the preparation, compounding, dispensing, and repackaging of radiopharmaceuticals. This chapter will be informational and not compendially applicable. Dec 1, 2020

Cabotegravir-rilpivirine

HIV-1 infection
Q1

Ponesimod

Relapsing MS
Q1

Ansofaxine HCl

Major depressive disorder
January

Dostarlimab

Endometrial cancer
Jan 14

Vericiguat

Heart failure
Jan 20

Casimersen

Duchenne muscular dystrophy
Feb 25

Melphalan flufenamide

Multiple myeloma
Feb 28

Paclitaxel and encequidar

Metastatic breast cancer
Feb 28

Ropeginterferon alfa-2b

Polycythemia vera
March

Fosdenopterin

Molybdenum cofactor deficiency
March

Aducanumab

Alzheimer disease
Mar 7

Taurolidine, heparin, and citrate (Defencath)

CRBSI
Mar 8

Arimoclomol

ALS
Mar 17

Idecabtagene vicleucel (bb2121, ide-cel)

Multiple myeloma
Mar 27

Dasiglucagon (Hypopal Rescue Pen)

Hypoglycemia
Mar 27

Tivozanib HCl

Metastatic renal cell carcinoma
Mar 31

Tanezumab

Osteoarthritis pain
Q2

Omblastys

Pediatric neuroblastoma
Apr 5

Leuprolide mesylate depot

Advanced prostate cancer
May 27

Umbralisib

Follicular lymphoma
Jun 15

Lonapegsomatropin

Growth hormone deficiency
Jun 25

Pegcetacoplan

Paroxysmal nocturnal hemoglobinuria
Q3

Selexipag

Pulmonary arterial hypertension
Q3

Belumosudil

Graft-vs-host disease
Q3

Teplizumab

Type 1 DM
July

Vosoritide

Achondroplasia
Aug 20

Loncastuximab tesirine

Diffuse large B-cell lymphoma
Sep 21

Management Standards for Hazardous Waste Pharmaceuticals (Part 266 Subpart P)

EPA final rule allows pharmaceutical reverse distributors and health care facilities that manage hazardous waste to exclude hazardous waste pharmaceuticals from regulation under the more stringent RCRA hazardous waste management standards

Jul 1, in authorized states that do *not* require a statutory amendment to adopt Subpart P

2021 Q1

Q2

Q3

Droxidopa

Northera
Feb 18

Pegfilgrastim (MSB11455)

Neulasta
Mar 27

Etravirine

Intelence
Jun 14

Formoterol fumarate

Perforomist
Jun 22

Sunitinib malate

Sutent
Aug 16

Nebivolol HCl

Bystolic
Sep 17

Ranibizumab (SB11)

Lucentis
Sep 18

Adalimumab (AVT02)

Humira
Sep 19

Cabazitaxel

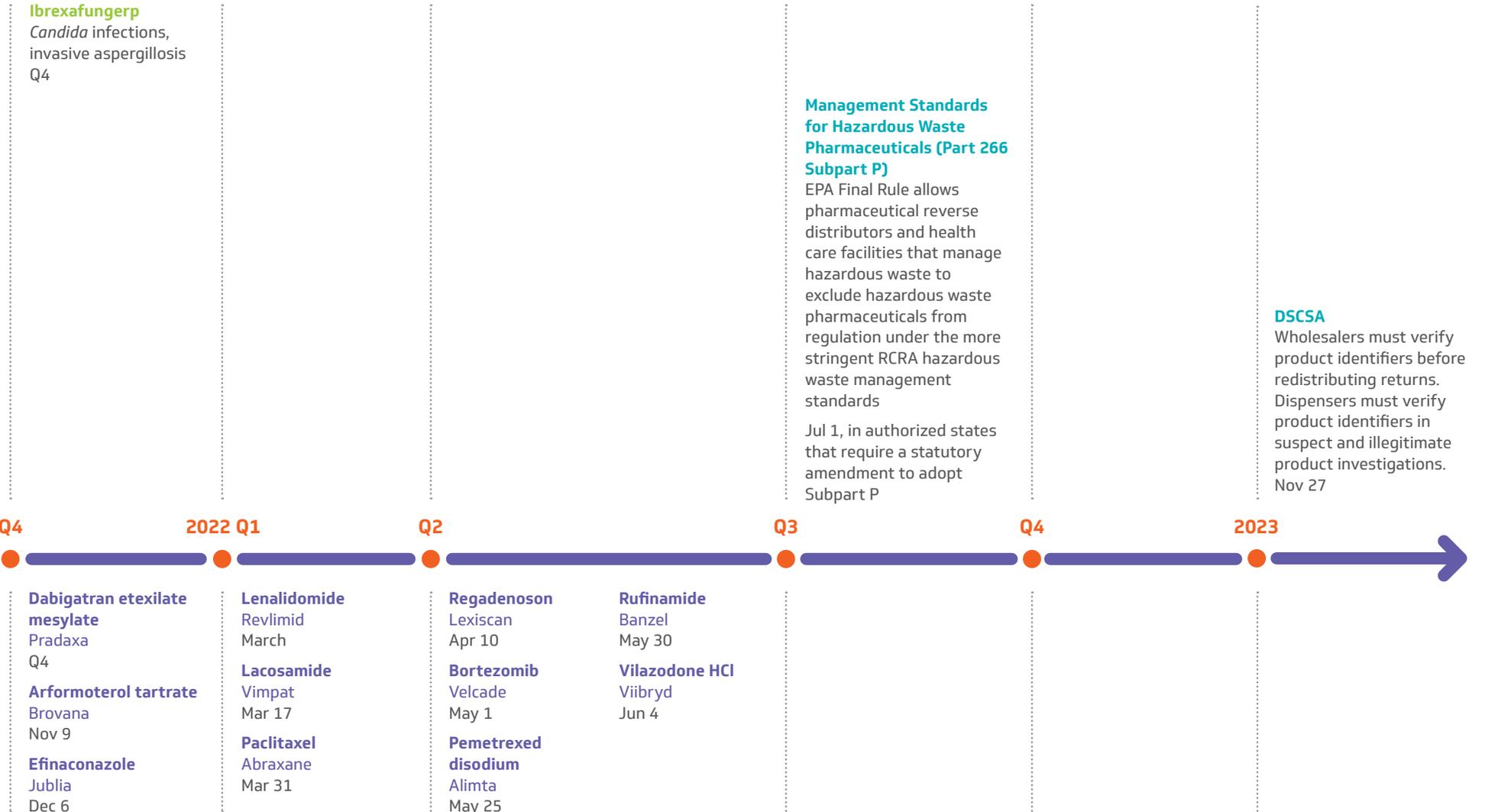
Jevtana kit
Sep 27

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

Abbreviations: ALS = amyotrophic lateral sclerosis; CRBSI = catheter-related blood stream infection; DM = diabetes mellitus; DSCSA = Drug Supply Chain Security Act; EPA = Environmental Protection Agency; MS = multiple sclerosis; PDUFA = Prescription Drug User Fee Act; RCRA = Resource Conservation and Recovery Act; USP = US Pharmacopeia.

Projected timelines and approvals

● New drug approvals ● Regulatory and accreditation events ● Anticipated availability of new generics and biosimilars^a



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

Abbreviations: ALS = amyotrophic lateral sclerosis; CRBSI = catheter-related blood stream infection; DM = diabetes mellitus; DSCSA = Drug Supply Chain Security Act; EPA = Environmental Protection Agency; MS = multiple sclerosis; PDUFA = Prescription Drug User Fee Act; RCRA = Resource Conservation and Recovery Act; USP = US Pharmacopeia.

Executive summary

The Winter 2021 Vizient Pharmacy Market Outlook includes our best estimate of the changes in the price of pharmaceuticals that Vizient Pharmacy Program participants will be purchasing between July 1, 2021, and June 30, 2022. The outlook focuses on pharmaceutical products used across multiple health system settings, including inpatient and non-acute, and provides a year-over-year estimate of expected price changes.

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 2 shows the percentage of member purchases and the estimated price changes by therapeutic class.

Without question, the COVID-19 pandemic continues to have an impact on clinical and financial outcomes. Throughout this report, you will see multiple examples of that influence. Still, the overall trend towards moderation of price increases persists, driven largely by some recent generic entrants as well as the expanding roster of approved and marketed biosimilars. Alongside this moderation, however, COVID-19 has led to increased use of high-cost drugs like vasopressin and tocilizumab. And even though substantial progress has been made on biosimilars, the largest contributor to drug price increases is still adalimumab — and projections suggest that will remain the case until 2023. Nevertheless, the trend toward more moderate drug price increases is welcome, given the financial difficulties created by the pandemic.

Table 1. Summary of projected drug price inflation, July 1, 2021-June 30, 2022

Product group	Vizient predicted price change, %	Percentage of analyzed group	Estimated price change weighted by Vizient purchases, %
Contract products	1.67	34.94	0.58
Noncontract products	3.21	65.06	2.09
Total weighted average drug price inflation estimate			2.67

Estimates based on Vizient member data for October 1, 2019-September 30, 2020.

Table 2. Estimated price change and percentage of Vizient member purchases by therapeutic class

Therapeutic class (subclass)	Key products in class	Class-estimated price change, %	Vizient membership purchases (percentage of analyzed group)
Antineoplastic agents	Keytruda, Rituxan, Opdivo	2.68	24.67
DMARDs	Humira, Remicade, Enbrel	4.65	11.79
Hematopoeitics	Neulasta, Aranesp, Udenyca	0.11	3.47
Immunomodulators (MS)	Ocrevus, Tysabri, Gilenya	2.04	2.82
Infectious diseases		2.70	11.23
Vaccines	Prevnar 13, Gardasil 9, Pneumovax 23	5.04	4.19
Antibacterials/antifungals (systemic)	Rifaximin, Daptomycin, Ertapenem	-0.19	3.64
HIV agents	Biktarvy, Genvoya, Triumeq	4.83	1.89
Hepatitis C agents	Eplclusa, Mavyret, Harvoni	0.14	1.22
Plasma critical care		3.10	4.25
Immune globulin, intravenous	Privigen, Gamunex-C, Gammagard	3.78	3.34
Albumin	AlbuRx, Albutein, Flexbumin	0.00	0.68

Vizient member data for October 1, 2019-September 30, 2020.

Abbreviations: DMARD = disease-modifying antirheumatic drug; MS = multiple sclerosis

Managing the impact of COVID-19 on budgeting

The projections in the Vizient Pharmacy Market Outlook are estimates of pricing behavior. In addition to price, utilization of medications is critical, particularly during the pandemic crisis. In 2021 as in 2020, members must remain aware of variations in medication use trends and their impact on total expenditures, especially as their communities experience surges of COVID-19 infection.

According to trends reported in the *American Journal of Health-System Pharmacy*, volume and mix for calendar year 2019 increased 10.9% in the clinic setting, but decreased 0.6% in the nonfederal hospital environment.¹ At the height of the COVID-19 outbreak, however, that pattern was reversed, as we noted in our Summer 2020 Drug Price Forecast. The *AJHP* article also reports that the change in total expenditures attributable to the introduction of new products in 2019 was 2.0% in the clinic setting and 1.3% for nonfederal hospitals.¹ Trends may be especially volatile and uncertain in 2021, given the introduction of more COVID-19 vaccines and therapies. Routine monitoring of spend and use patterns is strongly encouraged.

The estimates of price increases by therapeutic class offer further insight into the effects of price and utilization on drug spend. Oncology drugs and disease-modifying antirheumatic drugs (DMARDs) continue to dominate spending, as they have done for some years. However, the estimated price change for DMARDs is substantially higher as a result of the increases projected for adalimumab (Humira; AbbVie) and etanercept (Enbrel; Amgen); this pattern is expected to continue until effective biosimilar competition enters the market.

One area in which we see the impact of COVID-19 on manufacturing is in plasma-derived products. A shortage of plasma donors, resulting from the need for social distancing and restrictions on travel, has put more pressure on a market already facing supply challenges. As stated in our section on [critical care plasma agents](#), the plasma market will continue to tighten in 2021 and this will be reflected in the pricing for intravenous immune globulin (IgIV). Member organizations that have not already done so should review their mitigation strategies for limited IgIV supply.

Finally, it is critically important to understand another important dynamic for medications: the setting in which they are administered. While no price increase is desirable, the impact of such increases on overall financial performance differs depending on whether the product is administered in the inpatient setting (where drugs are generally not reimbursed separately) or outpatient setting (where drugs are separately reimbursed and also subject to substantial rebates). In the inpatient setting, there are a few situations in which price increases can be mitigated by reimbursement. As we have noted before, there is one prominent example that clearly illustrates negative financial consequences: vasopressin.

Across all classes of trade, the top spend medications for Vizient members (Table 3) are injectable medications administered or dispensed in some sort of non-acute setting (infusion center, specialty pharmacy) and separately reimbursed. However, among the top drugs by the size of their projected price increase (Table 4), the one drug that does not fit those criteria is vasopressin.

Table 3. Top 10 drugs by total spend among Vizient members (all classes of trade)

Rank	Generic drug name (brand name)
1	Adalimumab (Humira)
2	Pembrolizumab (Keytruda)
3	Rituximab (Rituxan)
4	Infliximab (Remicade)
5	Ustekinumab (Stelara)
6	Nivolumab (Opdivo)
7	Denosumab (Prolia, Xgeva)
8	Etelcalcetide hydrochloride (Parsabiv)
9	Ocrelizumab (Ocrevus)
10	Alteplase (Activase)

Vizient member data for October 1, 2019-September 30, 2020.

Table 4. Top 10 drugs by size of projected price increase

Rank	Generic drug name (brand name)
1	Adalimumab (Humira)
2	Vasopressin (Vasostriect)
3	Ustekinumab (Stelara)
4	Etanercept (Enbrel)
5	Pembrolizumab (Keytruda)
6	Vedolizumab (Entyvio)
7	Denosumab (Prolia, Xgeva)
8	Pneumococcal 13-valent conjugate vaccine (diphtheria CRM)/PF (Pevnar 13)
9	Secukinumab (Cosentyx)
10	Abatacept/maltose (Orencia)

Based on Vizient data.

Vasopressin, a vasoactive medication for critically ill patients with low blood pressure, is a decades-old drug that, prior to 2014, had never received formal approval from the Food and Drug Administration (FDA). As a result of the FDA's Unapproved Drugs Initiative (UDI), manufacturers of such legacy medications have been encouraged to seek formal approval and in turn have sometimes received a few years (3-5) of market exclusivity. However, the newly approved version of vasopressin included a formulation change that allowed the supplier to receive not only market

exclusivity, but patent protection, which extends to 2035. Immediately before the COVID-19 outbreak, Vizient communicated with many stakeholders, including the federal government, about the negative consequences of unintended loopholes like this that allow previously multisource drugs to be transformed into branded, single-source products for periods far longer than the normal exclusivities granted to truly new drugs.

On November 20, 2020, it was announced that the Department of Health and Human Services was ending the initiative.² Given the recent changes in leadership, the long-term implications of this decision are unknown, but Vizient has begun communications with the new administration and is continuing to engage with the FDA. For more information on our government relations efforts, see the [advocacy](#) section in this report.

During this time of crisis, it is helpful to see a moderation of price increases. However, the costs of pharmaceuticals in aggregate are so high that even small percentage increases can have a dramatic impact on health care organizations' financial performance. Therefore, it is critical for pharmacy leaders to be vigilant in accounting for all changes that have an impact on medication use and cost.

- 1 Tichy EM, Schumock GT, Hoffman JM, et al. National trends in prescription drug expenditures and projections for 2020. *Am J Health Syst Pharm.* 2020;77(15):1213-1230. doi:10.1093/ajhp/zxaa116.
- 2 Mezher M. HHS moves to end FDA's unapproved drugs initiative. *Regulatory Focus.* November 24, 2020. Accessed December 4, 2020. <https://www.raps.org/news-and-articles/news-articles/2020/11/hhs-moves-to-end-fdas-unapproved-drugs-initiative>

A closer look by segment

Acute care

It would be unfair to distill all of current acute care practice down to the management of COVID-19. At the same time, however, it is undeniable that the pandemic has had an overwhelming impact on the acute and critical care practice settings — and has therefore demonstrated how important it is to be able to deliver advanced intensive care for a sustained period of time and to have needed products (including drugs) available during an extended crisis. While management of COVID-19 in the acute care setting has been focused on investigational therapies such as the now-approved remdesivir (Veklury), emergency use authorizations for monoclonal antibodies, and investigational uses of existing therapies such as tocilizumab, an inordinate amount of attention and effort has been given to securing supplies of “essential” medications.

As has been noted many times and in many forums, drug shortages did not originate with COVID-19. The pandemic simply exacerbated an already fragile situation and illustrated the extent to which pharmacists and pharmacy technicians have been able to compensate for previous supply interruptions. Two critical Vizient missions have been rigorously scrutinizing the supply chain for the medications frequently used in COVID-19 management and expanding the Novaplus Enhanced Supply Program to include more **essential drugs**. To date, the Novaplus Enhanced Supply Program has grown to encompass more than 35 molecules, 165 NDCs, and 66 million additional protected units warehoused by manufacturers in the US, and has also provided more than \$306 million in warehousing cost avoidance for Vizient members. Vizient continues to expand the program, prioritizing essential medications identified by the Vizient clinical pharmacy team, and to work with other stakeholders to increase supply chain resiliency and maintain an ongoing dialogue with the FDA on the subject of essential medications. Currently, fill rates for most of the medications used in the management of COVID-19 have returned to a reasonable level of stability. Still, sustained vigilance and monitoring are needed.

COVID-19 costs

It may be impossible to quantify the total expense associated with COVID-19 across the health care system. Still, it is important to provide some context to the economic hardship. In the Summer 2020 Drug Price

Forecast, we estimated that the 10 most common critical-care drugs used in treating COVID-19 accounted for at least an additional \$200 million in pharmaceutical spend, based on a comparison of purchases for March-April 2020 with the same period the previous year. While the COVID-19 outbreak is by no means over, a continued review of the data shows a lessening, but still substantial, financial impact.

For May and June 2020, there was an overall decline in spend for many COVID-19–related drugs, likely because members had already invested in so much supply during the initial outbreak. However, a comparison of the third quarter of 2019 with the same period in 2020 shows purchases increasing again, although not by as much (Table 5). Five commonly used COVID-19–related drugs had measurable increases in purchases, totaling \$60.5 million in spend. Therefore the impact, though still significant, appears to be more manageable by the supply chain and by member organizations. Still, any additional cost is too much, particularly when dealing with medications given to inpatients, which are not reimbursed separately.

Table 5. Changes in inpatient drug spend during COVID-19

Drug name	Change in spend, %	Change in quantity purchased, %
Tocilizumab	92	32
Vasopressin	36	41
Cisatracurium	170	31
Dexmedetomidine	33	83
Propofol	6	-4

Based on comparison of Vizient member data for third quarter 2019 and third quarter 2020.

Price increases: inpatient vs outpatient

One effect of the pandemic has been to focus even more attention on the migration of treatment to non-acute or virtual settings to minimize the risk of infection and enable lower-cost care. However, COVID-19 has also highlighted the enduring necessity of providing high-quality critical care. As a result, understanding the dynamics of drug purchasing in a truly acute care framework is important.

Table 6 shows the 10 most commonly used medications for the acute care class of trade. Although they are identified as acute care, given the way in which members’ accounts

are structured within their distributor systems, the medications in this category include those used in the hospital or health system outpatient locations as well as in true acute care settings. Given their relative cost, these drugs — like the monoclonal antibodies and other biologics — dominate spend, even though they are also used in the non-acute environment. Unlike acute care medications, however, those administered in the outpatient setting are eligible for reimbursement. No increase in drug prices is desirable, but such increases can be mitigated to some extent when used in outpatient settings by the separate revenue chain. Conversely, medications administered in the inpatient setting are generally not eligible for separate reimbursement, so any increase in price for these drugs creates a direct loss that is not offset.

To illustrate the impact of this differentiation, Table 6 also illustrates the variations seen when evaluating all drugs normally captured for the hospital or health system and only those for which less than 5% of spend is in other classes of trade (e.g., retail, clinic, home infusion). In contrast to the biologic-heavy list based on total spend, this more narrowly tailored definition of acute care spend yields a top 10 list that includes alteplase, vasopressin, and sugammadex. It is important to consider both perspectives when assessing strategies to increase cost-effectiveness.

Table 6. Top 10 acute care drugs by total member spend

Rank	Drug name	
	Overall acute care	> 95% of sales in acute care class of trade
1	Pembrolizumab	Alteplase
2	Rituximab	Vasopressin
3	Alteplase	Sugammadex
4	Nivolumab	Albumin, human
5	Vasopressin	Acetaminophen
6	Pegfilgrastim	Antithymocyte globulin, rabbit
7	Immune globulin, gamma/proline/IgA 0-50 mcg/mL	Human prothrombin complex concentrate, 4-factor
8	Ocrelizumab	Bupivacaine liposome/PF
9	Infliximab	Calcitonin, salmon, synthetic
10	Adalimumab	Dexemedetomine HCl in 0.9% sodium chloride

Vizient member data for October 1, 2019-September 30, 2020.

The broader list demonstrates that biosimilar adoption must continue to be a source of focus for member organizations. The use of pegfilgrastim and infliximab continues to be eroded by competition. The same trend is expected for rituximab.

The more targeted definition of acute care drugs suggests that other products should be the focus of additional investigation. One such focus may be on the way to resolution: The recent launch of a generic competitor for injectable acetaminophen should have officially ended the era of high costs for this formulation. And hopefully there will be less need for vasopressin as COVID-19 is controlled and the number of critically ill patients decreases. While the White House announced that it intended to end the UDI initiative in November 2020, Vizient believes it is vital for additional manufacturers to enter the market for already-approved drugs (such as vasopressin) in order to increase competition and reduce potential supply disruptions. Finally, Vizient recently published the findings of an expert panel on the use of reversal agents in anticoagulation, which should help organizations with high spend for prothrombin complex concentrate and related product spend. In early 2021, Vizient will conduct a similar expert panel on the use of sugammadex.

Summary

COVID-19 has continued to alter our perspective on all forms and forums of care. The progress the health care system has made in providing essential care outside of the traditional hospital and health system environment in such a short time is impressive. However, we must also ensure that acute and critical care practices are able to withstand global crises such as a pandemic for a sustained period of time. We recommend that organizations pursue the following strategies:

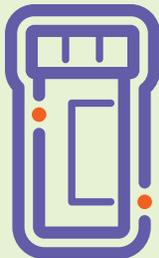
- **Use Novaplus and purchase all essential medications through the Novaplus Enhanced Supply Program.** The Vizient Novaplus program has a 3-decade history of offering market-leading value and promoting a more resilient supply chain. That level of resiliency has only increased with the launch and ongoing expansion of the Novaplus Enhanced Supply Program, which ensures additional US-based inventory of essential medications for Vizient members, with no additional fees or commitments. We will continue to expand the enhanced portfolio to include even more identified essential medications in an effort to minimize disruption and shortages.
- **Review essential medication lists.** The concepts behind the Novaplus Enhanced Supply Program and the development of the Vizient essential medications list predated the pandemic. However, both tools have served us well during this crisis. The FDA published its own version of an essential medications list for the first time in October 2020.¹ We encourage the use of the [Vizient Essential Medications Review](#), which is updated quarterly, and the FDA's list to develop disaster preparedness strategies.

- **Support continued biosimilar use.** As discussed in more detail in the [biosimilars](#) section of this report, we have reached a critical threshold for expanded realization of savings for biologic drugs. Even for care provided within the hospital, biosimilars can offer substantial savings. Therefore, plans to adopt biosimilars should be accelerated.
- **Take advantage of advocacy opportunities.** Vizient continues to advocate for legislative and regulatory changes to advance goals such as ending drug shortages, supporting biosimilar development, or ensuring an

effective response to COVID-19. We recommend you reach out to your colleagues in government relations to ensure their awareness of pharmacy policy issues.

1 Executive order 13944: List of essential medicines, medical countermeasures, and critical inputs. Food and Drug Administration. Updated October 30, 2020. Accessed December 4, 2020. <https://www.fda.gov/about-fda/reports/executive-order-13944-list-essential-medicines-medical-countermeasures-and-critical-inputs>

Specialty pharmaceuticals



4.25%

Specialty drug inflation rate

Since July 2019, Vizient has included projections for specialty drug prices in our market outlook publications. However, evaluating these medications can be challenging as there is no standard definition of a specialty drug. Comparing the definitions and specialty drug lists¹⁻⁷ provided by some of the nation’s top payers (United Health, Anthem, and Aetna), the Centers for Medicare & Medicaid Services (CMS), and specialty pharmacies (Walgreens and CVS) reveals many differences in the criteria used to define a specialty drug. For instance, CMS currently specifies a cost of \$670 per month per patient,⁸ whereas other organizations may only use nonspecific terms like “high cost” or may not use cost as a criterion at all.

For the purposes of our projection, Vizient worked with IPD Analytics to establish criteria defining specialty drugs as those that (1) are used to treat rare or orphan diseases, (2) are high cost (defined as more than \$4,000 per patient per month), (3) require a specialist prescriber, (4) are “high touch” — that is, require frequent clinical monitoring for safety and efficacy, or (5) have limited distribution. Using this definition, 141 unique drugs and 796 National Drug Code numbers (NDCs) were identified for our analysis. We applied historical trends, market conditions, and member spend data to prices for these drugs, replicating the methodology used for the overall Pharmacy Market Outlook.

The resulting predicted price inflation for specialty products is 4.25% (Table 7). Separate examination of biologic and nonbiologic products, based on FDA approval type, indicates a shift towards increased spend on biologic products, in contrast to the more equal division of spend we found in the summer 2020 forecast.

The specialty drug inflation rate is higher than the predicted overall rate of 2.67%. Considering that prices of specialty drugs already tend to be higher than those of nonspecialty items, this finding suggests that budgeting for specialty products will be especially important for our members in the next 18 months.

How does the lack of a standard definition affect projections?

The lack of a standard definition of a specialty product has resulted in different specialty drug lists from stakeholders such as specialty pharmacies, payers, and CMS. We investigated how projections based on these different lists — each with a unique combination of drugs and NDCs — would change the predicted specialty drug inflation rate. Our findings are shown in Table 8.

Table 7. Estimated specialty drug price inflation rates for July 1, 2021-June 30, 2022

Product group	Vizient predicted price change, %	Percentage of analyzed group	Estimated price change weighted by Vizient purchases, %
Biologics	4.61	85.87	3.96
Nonbiologics	2.08	14.13	0.29
Total weighted average drug price inflation estimate			4.25

Estimates based on Vizient member data for October 1, 2019-September 30, 2020.

Table 8. Estimated specialty drug price inflation rates for specific specialty drug lists, July 1, 2021-June 30, 2022

Product group	Estimated price change by specialty drug list owner, %			
	CMS	Walgreens/CVS (combined)	Private payers ^a (combined)	Vizient
Biologics	2.56	2.28	2.35	3.96
Nonbiologics	1.17	0.69	0.58	0.29
Total weighted average drug price inflation estimate	3.73	2.97	2.92	4.25

Estimates based on Vizient member data for October 1, 2019-September 30, 2020.

^a Private payers include Aetna, Anthem, and United Healthcare.¹⁻⁴

It is our hope that validations of these projections can provide much-needed insight into the best definition of specialty products, at least for the purposes of forecast analytics.

Summary

Specialty pharmaceuticals continue to dominate both drug approvals and purchasing. We know that our members must measure their successes in terms of cost, quality, and market performance, and that this is especially true in the context of specialty pharmacy practice. The fact that many specialty products are high cost and that we are predicting an inflation rate for this drug category that is higher than the overall rate means that a defined specialty pharmacy strategy will be important for our members in the months and years ahead. Vizient and **Acentrus Specialty™** are working to enhance our offerings to address every aspect of this market and provide solutions to the challenges our members face in managing this segment of the market.

- 1 Specialty drug coverage: 2020 Aetna specialty drug list. Aetna. October 2020. Accessed October 27, 2020. <http://www.aetna.com/individuals-families-health-insurance/document-library/pharmacy/2020-comprehensive-specialty-pharmacy-drug-list.pdf>
- 2 Exclusive specialty drug list. Anthem. Updated May 1, 2020. Accessed October 27, 2020. https://file.anthem.com/44150MUMENABS_IGX.pdf
- 3 Your 2021 prescription drug list: traditional 4-tier. United Healthcare. October 2020. Accessed October 27, 2020. <https://www.uhc.com/content/dam/uhcdotcom/en/Pharmacy/PDFs/Traditional-4-Tier-PDL-Eff-Jan-1-2021.pdf>
- 4 Your 2020 prescription drug list: advantage 4-tier. United Healthcare. April 2020. Accessed October 27, 2020. <https://www.uhc.com/content/dam/uhcdotcom/en/Pharmacy/PDFs/Traditional-4-Tier-PDL-Eff-May-1-2020.pdf>
- 5 CVS Specialty Pharmacy distribution drug list. CVS Specialty. Updated October 2020. Accessed October 15, 2020. <https://www.cvsspecialty.com/education-center/downloads/SpecialtyDrugs.pdf>
- 6 Specialty pharmacy drug management list. Prime Therapeutics LLC. Updated October 1, 2020. Accessed October 15, 2020. https://www.myprime.com/content/dam/prime/memberportal/forms/2020/FullyQualified/Other/ALL/BCBSAL/COMMERCIAL/ALL/AL_Specialty_Drug_List.pdf
- 7 Medicare Plus Blue PPO: 2020 Plus comprehensive formulary. Blue Cross Blue Shield of Michigan. Updated October 1, 2020. Accessed October 19, 2020. <https://www.bcbsm.com/content/dam/microsites/medicare/documents/2020/pharmacy/ppo-formulary-comprehensive-plus.pdf>
- 8 Restructuring Medicare Part D for the era of specialty drugs. In: Medicare Payment Advisory Commission. June 2019 Report to the Congress: Medicare and the Health Care Delivery System. MedPAC. June 2019. Accessed October 20, 2020. http://www.medpac.gov/docs/default-source/reports/jun19_ch2_medpac_reporttocongress_sec.pdf

Non-acute care

As with every other aspect of health care, our discussion of the state of the non-acute market begins with the impact of the COVID-19 pandemic. While non-acute pharmacy practice has been a critical part of health care since long before COVID-19, the pandemic has reinforced the importance of clinical practice services not directly associated with a hospital or health system structure. The ability to deliver coordinated medication management services in non-acute settings, including the administration of monoclonal antibodies to treat COVID-19, is essential to any pandemic recovery strategy.

The COVID-19 crisis has also posed unique challenges for non-acute providers. On the one hand, patients' reluctance to go to hospitals as well as the shortage of hospital beds resulting from the need to devote resources to critical care services have created a tremendous opportunity for non-acute providers. However, protecting clinicians, staff, and the patients they serve is no less of a concern outside of a hospital. A late-summer Provista® survey on resumption of elective procedures¹ found that ambulatory surgery center members were most worried about:

- Supply chain issues
- A second wave of infection
- Choosing the appropriate caseload for the time period
- COVID-19 testing turnaround time
- Patients' willingness to return
- Requirements for social distancing and guidelines from the Centers for Disease Control and Prevention (CDC)
- Staff safety

Non-acute care, even as it helps compensate for lost hospital- or health system-directed care, has continued to face similar hurdles in terms of protecting patients and staff.

Home infusion pharmacy and telepharmacy

Of the aspects of care that have received the most attention during the pandemic, expansion of home infusion services and the ability to leverage virtual access to pharmacist expertise via telepharmacy have been among the most discussed. That is not a surprise: Given the increase in health care consumerism, it is logical that patients, independent of pandemic concerns, would prefer to receive treatment in the comfort of their own homes whenever possible. Telepharmacy like telemedicine, also offers a way to overcome long-standing limitations on access points for basic patient care services.

The expectation is that both home infusion and telepharmacy services will continue to grow. Many high-cost medications are delivered via infusion and more similar products are in development. One of the biggest challenges for high-cost infused chemotherapy agents is whether they can be administered at home.² Finding mechanisms to ensure safe home infusion for these drugs is therefore an important issue. The competencies, technologies, and skills needed to deliver telepharmacy services will continue to expand and major pharmacy practice organizations are providing education, guidance, and resources for this evolving area of practice.^{3,4}

COVID-19 vaccines and therapies in the non-acute market

To date, the FDA has granted emergency use authorization for 2 COVID-19 vaccines.⁵ Hospitals and health care systems will, of course, play a prominent role in the delivery and administration of vaccines. However, physician offices, ambulatory care clinics, and retail pharmacy practices are critically important, especially as more doses become available. It is essential for all care outlets that can assist in vaccination to be prepared to do so. To support this preparation, the Vizient **Vaccine Resource Center** offers the latest information and resources on vaccine development and distribution. Beyond vaccines, non-acute facilities have been and will remain the primary avenue for the delivery of the monoclonal antibodies targeting COVID-19 to limit disease progression in patients and save desperately needed hospital beds.

Top spend medications

The top spend drugs in the non-acute setting remain consistent (Table 9). As in previous editions of this report, adalimumab preserves its status as the top-spend drug, followed by an array of familiar oncology products, immunomodulators, and other related medications. It is anticipated that US spend for adalimumab will exceed \$24 billion in 2020, and that biosimilar competition will not enter the market until 2023.^{6,7} As noted in the **biosimilars** section, uptake of competitors for branded biologics has continued to grow as more options have entered the market. Efforts to encourage biosimilar use must continue to promote both prescriber confidence and patient acceptance.

Table 9. Top 10 drugs by non-acute spend for Vizient members

Rank	Drug name
1	Adalimumab
2	Etelcalcetide
3	Infliximab
4	Etanercept
5	Denosumab
6	Pembrolizumab
7	Rituximab
8	Secukinumab
9	Abatacept
10	Ocelizumab

Vizient member data for October 1, 2019–September 30, 2020.

We project that the price of these top-spend medications will increase by 0% to 8%. The introduction of biosimilars for infliximab and rituximab has arrested price increases for these drugs, in contrast to adalimumab and etanercept, for which biosimilar competition has been delayed. The only other product for which there could be a competitor in the near term is secukinumab. Phase 3 trials are presently under way for a possible competitor that could become available in 2023; however, this timeline is subject to tremendous litigation hurdles.⁷ Therefore, it is not surprising that the projected price increase for this product is comparable to those for adalimumab and etanercept. More information on other patent expirations and exclusivities can be found in the [timeline](#).

Recovery of other non-acute spend

Just as patient visits and procedures have returned to more routine levels, so has the purchase of many common non-acute drugs, including routine vaccines. Both this and the apparent increased level of interest in 2020–2021 seasonal influenza vaccines are very positive changes. However, more work is needed to minimize any lingering negative impact of COVID-19 on demand for vaccines, which in some cases decreased by 95% at the height of the pandemic.⁸ The section on [vaccines](#) offers more information and insights on this topic.

The role of non-acute providers in the future of health care

Pharmacists in the non-acute care sector will continue to play a definitive role in the future of health care — managing the ongoing impacts of the pandemic, accommodating the demand for easier access to care, and strategizing ways to cope with increasing drug costs. Ongoing challenges include identifying the best mechanisms and most appropriate solutions to meet unique population needs and ensuring appropriate reimbursement for expansion of essential services. Strategic priorities for non-acute providers in the next 6 to 18 months include:

- **Planning and preparing to receive and administer vaccines and therapies for COVID-19.** Until a majority of the population has been vaccinated, controlling infection spread will remain time consuming and labor intensive. Health systems and hospitals will take the lead in disseminating vaccines, especially since guidance by a federal advisory panel of the CDC on December 2 stated that the estimated 21 million health care workers have priority, along with long-term care facilities. However, as more vaccines become available, physicians’ offices, ambulatory care clinics, and retail pharmacies will need to be able to step up. In addition, the recently authorized monoclonal antibodies bamlanivimab, casirivimab, and imdevimab are intended to be given outside of the hospital setting,⁹ and authorization of other such products is expected to follow.
- **Leveraging the capabilities of home infusion pharmacy.** The lingering effects of the pandemic and increased consumerism in health care will continue to place a substantial premium on ease of access to critical treatments. Providers must continue to advocate for appropriate reimbursement to expand this area of practice and work to define when such services are appropriate for the oncology population.
- **Expanding use of technology to increase access.** Providers must ensure that their capacity to connect with patients is not restricted by a need for in-person engagement. Non-acute providers must have technical capabilities and an understanding of regulatory considerations to increase their ability to deliver care virtually, including via telepharmacy.

Vizient and Provista are always available to help non-acute providers navigate the dynamics of both crisis circumstances, such as a global pandemic, and day-to-day practice to find the best solutions for their patient populations.

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- 2 Oncology home infusions in the post-COVID-19 world. AVBCC COVID-19 webcast series. JHOP Online: web exclusives. Updated July 21, 2020. Accessed November 8, 2020. <http://jhonline.com/ton-web-exclusives/18258-oncology-home-infusion-in-the-post-covid-19-world>
- 3 Alexander E, Butler CD, Darr A, et al. ASHP statement on telepharmacy. *Am J Health Syst Pharm*. 2017;74(9):e236-e241.doi:10.2146/ajhp170039
- 4 Telehealth during COVID-19. American Pharmacists Association. Accessed November 8, 2020. <https://www.pharmacist.com/coronavirus/telehealth>
- 5 COVID-19 vaccines authorized for emergency use. COVID-19 Vaccines. Food and Drug Administration. Updated December 22, 2020. Accessed December 28, 2020. <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines>
- 6 IQVIA SMART Solutions database. IQVIA; 2020. Accessed November 8, 2020. www.iqvia.com
- 7 IPD Analytics LifeCycle Biologics database. IPD Analytics; 2020. Accessed November 8, 2020. www.ipdanalytics.com
- 8 Issue brief: The impact of COVID-19 on US vaccination rates. National Foundation for Infectious Diseases. Accessed November 8, 2020. <https://www.nfid.org/keep-up-the-rates/issue-brief-the-impact-of-covid-19-on-us-vaccination-rates/#:~:text=An%20analysis%20from%20VaxCare%20found,declines%20of%20more%20than%2060>
- 9 Coronavirus (COVID-19) update: FDA authorizes monoclonal antibody for treatment of COVID-19. News release. Food and Drug Administration; November 9, 2020. Accessed November 9, 2020. <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-mono-clonal-antibody-treatment-covid-19>

Pediatrics



2.88%

Pediatric inflation rate

Unlike most areas of patient care, the pediatric segment has been less affected by the COVID-19 pandemic. Most routine health service appointments and vaccinations got back on track last summer for patients over 6 years of age, although the group under 6 is still behind on both vaccinations and well visits.¹ Overall, the greatest impact of COVID-19 for this population has been slowing of the approval of high-cost drugs for rare diseases.

Drug approvals for the pediatric population are still primarily in 3 categories: specialty drugs, gene therapy, and chimeric antigen receptor (CAR) T-cell treatments. All three present budgetary and revenue capture obstacles, requiring additional evaluation before including them in hospital formularies. Value-based approaches to evaluating these treatments include quality-adjusted life years, outcomes-based payments and indication-based pricing.²

Approximately 80% of known rare diseases are based on genetic mutations, and gene therapies led the high-cost target drug list in pediatrics in 2019 and 2020. It is difficult to quantify their impact on pediatric hospital budgets because of the way these treatments are distributed.

Recent approvals

In August 2020 the FDA approved viltolarsen (Viltepso; NS Pharma), an antisense oligonucleotide for patients with Duchenne muscular dystrophy (DMD) that is amenable to exon 53 skipping.³ DMD is a genetic disorder characterized by progressive muscle degeneration due to genetic alterations in the production of dystrophin protein.⁴

Risdiplam (Evrysdi [RG7916]; Genentech) was approved⁵ as an oral alternative to intrathecal nusinersen (Spinraza; Biogen) and intravenous (IV) onasemnogene abeparvovec-xioi (Zolgensma; Novartis) for the treatment of spinal muscular atrophy (SMA). The availability of a gene therapy alternative that enables convenient at-home administration will be pivotal to parents and patients. For hospitals, the impact of the new alternative will be to decrease both revenue from and costs for nusinersen and onasemnogene abeparvovec-xioi. The pricing strategy for risdiplam offers price parity with nusinersen, with a maximum yearly cost of \$400,000. The \$2.1 million cost of a single infusion of onasemnogene abeparvovec-xioi sets a high cost threshold among SMA treatments.⁶

AveXis is currently awaiting approval from the FDA to resume studying intrathecal administration of onasemnogene abeparvovec-xioi, a gene therapy for treatment of SMA. The study was halted in late 2019 because of dorsal root ganglia mononuclear inflammation seen in animal studies⁷; however, the therapy is still available as an IV infusion for patients with type 1 SMA. For patients with types 2 and 3 SMA, intrathecal nusinersen and oral risdiplam can be administered.⁸

Cost increases driven by specialty drugs, outpatient care

Pediatric pharmaceutical costs are rising as a result of the targeting of rare diseases that require specialty or orphan drugs. Based on purchase data for self-governed children's hospitals that participate in the Vizient Pharmacy Program, we predict the inflation rate for pediatric pharmaceuticals to be 2.88%.

Table 10 lists the top 10 drugs based on total expenditures among self-governed children's hospitals, the drugs' ranking from the January 2021 Pharmacy Market Outlook and overall spend among Vizient members for January 1

through September 30, 2020. Dinutuximab (Unituxin; AbbVie), indicated for high-risk neuroblastoma, has been the highest-spend drug for several years. Similarly, pegaspargase (Oncaspar; Shire), a modified enzyme used to treat acute lymphoblastic leukemia, and infliximab (Remicade; Janssen Biotech), a monoclonal antibody used in the treatment of autoimmune diseases, have remained in the top 3 for year-over-year spend.

New to the top 10 is empalumab-lzsg (Gamifant; Sobi), indicated for the treatment of hemophagocytic lymphohistiocytosis, which occurs when histiocytes and lymphocytes are overstimulated in response to bacteria or viruses, leading to increased cytokine production and causing cytokine storms and rapid decompensation. Empalumab-lzsg has a wholesale acquisition cost (WAC) of \$16,885 per 50-mg vial (\$340/mg). At weight-based dosing (starting at 1 mg/kg every 2-3 days based on response) for a 9-kg patient, an average starting dose is \$3,040.⁹

Defibrotide (Defitelio; Jazz Pharmaceuticals), indicated for the treatment of hepatic veno-occlusive disease (also known as sinusoidal obstruction syndrome), was new to the top 10 last year and remains there in 2021.¹⁰

Table 10. Top 10 pediatric drugs based on spend^a among self-governed children's hospitals that participate in the Vizient group purchasing organization

Current ranking among children's hospitals ^b	Previous ranking among children's hospitals ^c	Generic drug name (brand name)
1	1	Dinutuximab (Unituxin)
2	3	Infliximab (Remicade)
3	2	Pegaspargase (Oncaspar)
4	4	Palivizumab (Synagis)
5	6	Defibrotide sodium (Defitelio)
6	7	Pneumococcal 13-valent conjugate vaccine (Prevnar-13)
7	8	Eculizumab (Soliris)
8	4	Asparaginase (Erwinaze)
9	--	Empalumab-lzsg (Gamifant)
10	10	Pegfilgrastim (Neulasta)

^a 340B purchases were excluded from the analysis.

^b Based on data for January 1-September 30, 2020.

^c Ranking from July 2020 Drug Price Forecast based on data for September 1, 2018-August 31, 2019.

In the pipeline

As noted earlier, the greatest impact of COVID-19 on the pediatric pharmaceutical pipeline has been to delay or suspend research on potential medications. A recent statement from Bluebird Bio said that the biologics license application (BLA) for its LentiGlobin gene therapy for beta-thalassemia will be delayed until mid-2021 because of COVID-19. With this delay, however, the company will be able to broaden the patient population to include beta⁰/beta⁰ genotypes and pediatric patients.¹¹

Moderna Therapeutics, which focuses on messenger RNA (mRNA) therapy for a wide range of rare diseases, has halted its pediatric respiratory trials to focus on COVID-19 vaccine production. Moderna was close to starting phase 2 trials for treatments for respiratory syncytial virus and phase 1 trials for phenylketonuria and type1a, G6Pase glycogen storage disorders.¹²

Jazz Pharmaceutical is working to obtain fast-track designation for its recombinant asparaginase (JZP-458). Early results from a phase 2/3 study were presented at the American Society of Clinical Oncology's annual meeting in May and June 2020. Quick release of this product will provide relief in an area that has been plagued with shortages.¹³

On August 25, 2020, the FDA accepted the new drug application for casimersen (Amondys 45; Sarepta Pharmaceuticals) for the treatment of DMD. Casimersen is a type of gene therapy — antisense oligonucleotide — that improves the outcomes of protein synthesis by hiding the mutations in the mRNA at exon 45, allowing the cell to overcome the mutation and produce dystrophin protein that is partially functional.¹⁴

Table 11 lists products currently in development, some of which are expected to carry substantial costs.

Table 11. Important late-phase investigational drugs with pediatric studies ongoing

Generic drug name/ID (brand name)	Clinical trial phase	Manufacturer	Indication	COVID-19 impact
Remistemcel-L (Ryoncil)	4	Mesoblast	Pediatric steroid-refractory GVHD	Also in phase 3 trials for ARDS
Ataluren (Translarna)	4	PTC Therapeutics	DMD	None
JZP458: recombinant <i>Erwinia</i> asparaginase	2/3	Jazz Pharmaceutical	Acute lymphoblastic leukemia, lymphoblastic lymphoma	None
Casimersen/SRP-4045 (Amondys 45)	3	Sarepta Pharmaceuticals	DMD	None
Valoctocogene roxaparvovec/BMN 270 (Roctavian)	3	Biomarin Pharmaceutical	Hemophilia A	None
LentiGlobin (Zynteglo)	3	Bluebird Bio	Beta-thalassemia and sickle cell disease	Development and release delayed until mid-2021

Data derived from Maese et al, Gurunathan, Sarepta, ClinicalTrials.gov, and Cure SMA.¹³⁻¹⁷

Abbreviations: ARDS = acute respiratory distress syndrome; DMD = Duchenne muscular dystrophy; GVHD = graft-versus-host disease.

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- 2 Kaltenboeck A, Bach PB. Value-based pricing for drugs: theme and variations. *JAMA*. 2018;319(21):2165-2166.
- 3 Viltepsio (viltolarsen). Package insert. NS Pharma; August 2020.
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- 6 Pagliarulo N. Zolgensma set a new drug pricing bar: insurers show some signs of pushback. *BioPharma Dive*; July 3, 2019. Updated July 5, 2019. Accessed June 30, 2020. <https://www.biopharmadive.com/news/zolgensma-set-a-new-drug-pricing-bar-insurers-show-some-signs-of-pushback/558101>
- 7 Novartis announces AVXS-101 intrathecal study update. News release. Novartis-AveXis; October 30, 2019. Accessed June 2020. <https://www.avexis.com/news-releases/news-release-details/novartis-announces-avxs-101-intrathecal-study-update.html>
- 8 Spinraza (nusinersen). Package insert. Biogen; 2016-2019.
- 9 Gamifant (emapalumab-izsg). Package insert. Sobi; 2019.
- 10 Defitelio (defibrotide sodium). Package insert. Jazz Pharmaceuticals; 2016.
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- 13 Maese L, Rau RE, Raetz EA, et al. A phase II/III study of JZP-458 in patients with acute lymphoblastic leukemia (ALL)/lymphoblastic lymphoma (LBL) who are hypersensitive to *E. coli*-derived asparaginases. *J Clin Oncol*. 2020;38(15 suppl): Abstract TPS7568. doi:10.1200/JCO.2020.38.15_suppl.TPS7568
- 14 Gurunathan S. FDA accepts Sarepta therapeutics' new drug application for DMD treatment casimersen. Muscular Dystrophy Association. August 26, 2020. Accessed October 18, 2020. <https://strongly.mda.org/fda-accepts-sarepta-therapeutics-new-drug-application-for-dmd-treatment-casimersen>
- 15 COVID-19 resources for patients and families. Sarepta Therapeutics. April 11, 2020. Accessed June 18, 2020. <https://www.sarepta.com/community-update-covid-19>
- 16 Duchenne muscular dystrophy clinical trials. ClinicalTrials.gov Accessed June 28, 2020. 2020. <https://clinicaltrials.gov/ct2/results?cond=Duchenne+Muscular+Dystrophy&term=&cntry=&state=&city=&dist=>
- 17 SMA drug pipeline. Cure SMA. Accessed June 2020. <https://www.curesma.org/sma-drug-pipeline>



Key therapeutic class summaries

Oncology

2.68%

Period projected
inflation rate

24.67%

Portion of drug spend

Impact of COVID-19 on cancer treatment

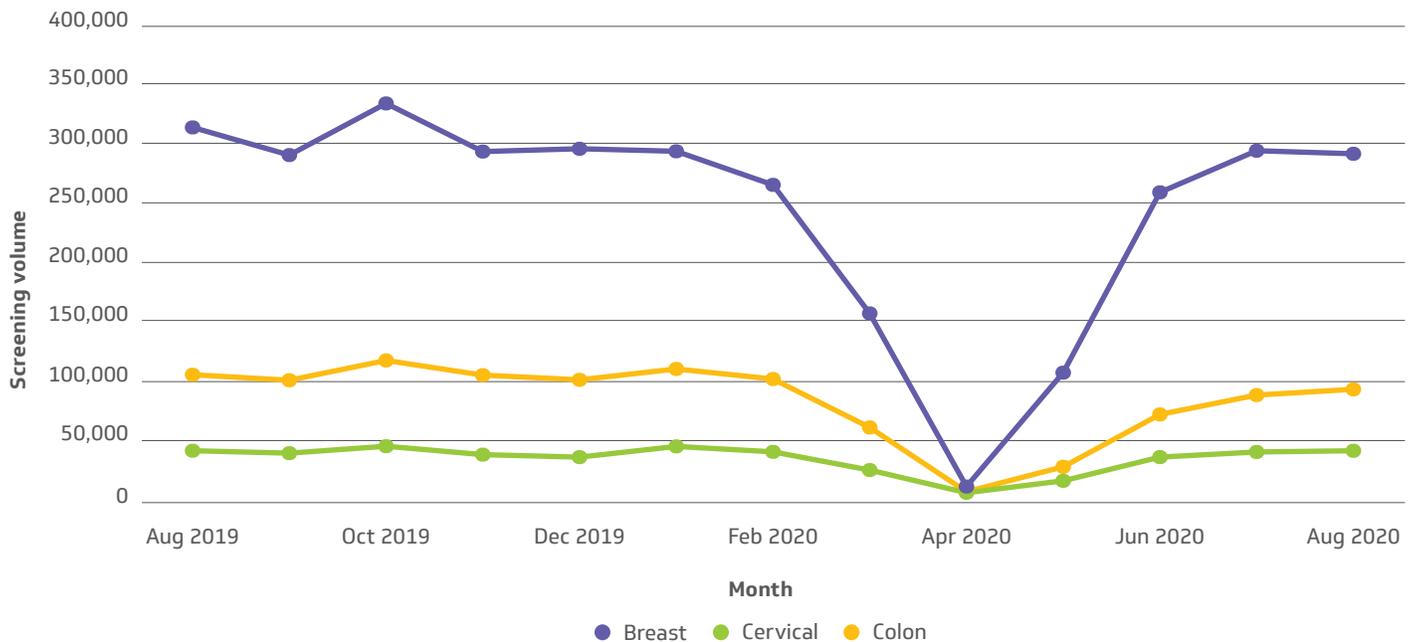
It has been suggested that cancer patients could have a more serious response to COVID-19 than the general population because of their immunocompromised state. The lack of robust information and data on mortality rates, severity, and the association with tumor subtype for patients who tested positive for COVID-19 has left those caring for cancer patients wondering how best to proceed with treatments and procedures for cancer diagnoses. There are multiple studies aggregating severity and outcomes of COVID-19 in cancer patients, but mortality rates in these studies have not been consistent. However, they do reinforce the finding that age is a significant determinant of severity of illness, regardless of comorbidities. One clinical trial reported that cancer patients with no comorbidities had a mortality rate of approximately 4%; for those with progressive disease the mortality rate was 26%.¹ In patients 75 years and older the mortality rate was 27%; for older patients with an Eastern Cooperative Oncology Group (ECOG) performance status of 2 or greater, it was 35%.¹ The long-term impact of COVID-19 on cancer patients remains a critical metric to track in weighing the implications and considerations for treatment timing in this patient population.

Trends in oncology preventative screening and services

At the height of the pandemic, cancer screening protocols were put on hold as patients remained at home and in-person visits were converted to telehealth communications. It is estimated that breast cancer screenings dropped by 89.2% and colorectal cancer by 84.5%, which contributed to a 65.2% decline in the incidence of new cancer diagnoses as of May 2020.² Delays in detection and diagnosis of cancer can have a significant impact on patient outcomes. Prospective quantitative modeling estimates there will be a 7.9% to 9.5% increase in deaths from breast cancer within 5 years of diagnosis and a 15.5% to 16.6% increase in colorectal cancer deaths.²

Data from the Vizient Clinical Data Base for non-inpatient cancer screenings between August 2019 and August 2020 show that screening rates for breast, colon, and cervical cancer have recovered since the height of the first COVID-19 surge, to 98.7%, 87.9%, and 101.7%, respectively, of the average monthly volume from September 2019 to February 2020 (Figure 1). (The Vizient Clinical Data Base is an analytic platform for performance improvement populated by hundreds of health systems and community hospitals nationwide, including nearly all academic medical centers. It includes comparative data for benchmarks such as demographic, mortality, length of stay, complication rates, readmission rates, diagnosis, procedure, resource utilization and more.)

Figure 1. Post-COVID-19 recovery of non-inpatient screenings for breast, colon and cervical cancer



Data from the Vizient Clinical Data Base. All rights reserved. Participating hospitals with at least 1 screening in March 2020. Includes non-inpatients ≥ 18 years old with ICD-10 codes Z12.31 (432 hospitals), Z12.4 (290 hospitals), and Z12.11 (485 hospitals).

To examine rates of recovery for inpatient oncology services, we retrieved data for Medicare severity diagnosis-related group (MS-DRG) codes for the top 5 inpatient oncology and surgical oncology sub-service lines — gastroenterology, genitourinary, thoracic, gynecology, and otolaryngology/oral — for January-August 2020. The overall rate of service recovery for medical and surgical

oncology is 95% as of August 2020. Table 12 shows the decrease and recovery for the service lines examined. Anecdotally, financial leaders and administrators from Vizient member organizations have estimated that overall service recovery will fall within 10% of baseline from pre-COVID-19 levels.

Table 12. COVID-19 impact on medical and surgical oncology sub-service lines decrease and recovery

Service line	Medical		Surgical	
	Decrease (March-April), %	Recovery from average (August), %	Decrease (March-April), %	Recovery from average (August), %
Overall	26	95	33	95
Gastroenterology	27	97	34	95
Genitourinary	20	93	32	92
Thoracic	22	100	38	91
Gynecologic	26	97	38	98
ENT/oral	25	93	21	95

Data from Vizient Clinical Data Base. All rights reserved. 522 participating hospitals, January-August 2020. Abbreviation: ENT = ear, nose, throat.

Oncology drug spending

Table 13 shows oral and IV oncology products that have seen the greatest price change, based on Vizient member data for October 2019 through September 2020.

Pembrolizumab (Keytruda; Merck) and nivolumab (Opdivo; Bristol Myers Squibb) were each approved by the FDA for 5 additional indications in 2020. Pembrolizumab can now be administered for 18 different cancer disease states, including 2 predictive biomarkers, while nivolumab can be used for 11 indications. Use of pembrolizumab therefore continues to outpace nivolumab; pembrolizumab now accounts for the second-highest amount of spend for Vizient members.

Other antineoplastic products with significant change in price for the period January–September 2020 compared with the same period in 2019 are polatuzumab vedotin-piicq (Polivy; Genentech), approved in June 2019 for the treatment of large B-cell lymphoma; alpelisib (Piqray; Novartis), approved in May 2019 for breast cancer; and selinexor (Xpovio; Karyopharm Therapeutics), approved in July 2019 for multiple myeloma and diffuse large B-cell lymphoma.

Table 13. Change in utilization, spend, and price for oncology medications

Drug name	Utilization change	Change in Vizient member spend	WAC change, %
Intravenous			
Atezolizumab	↑	↑	2.0
Ado-trastuzumab	↓	↑	3.0
Pegaspargase	↓	↑	9.4
Bendamustine	↓	↓	5.0
Oral			
Ruxolitinib	↑	↑	3.0
Venetoclax	↑	↑	5.0
Abiraterone	↑	↓	0
Olaparib	↑	↑	1.0
Nilotinib	↑	↑	7.0
Imatinib	↓	↓	-57.0

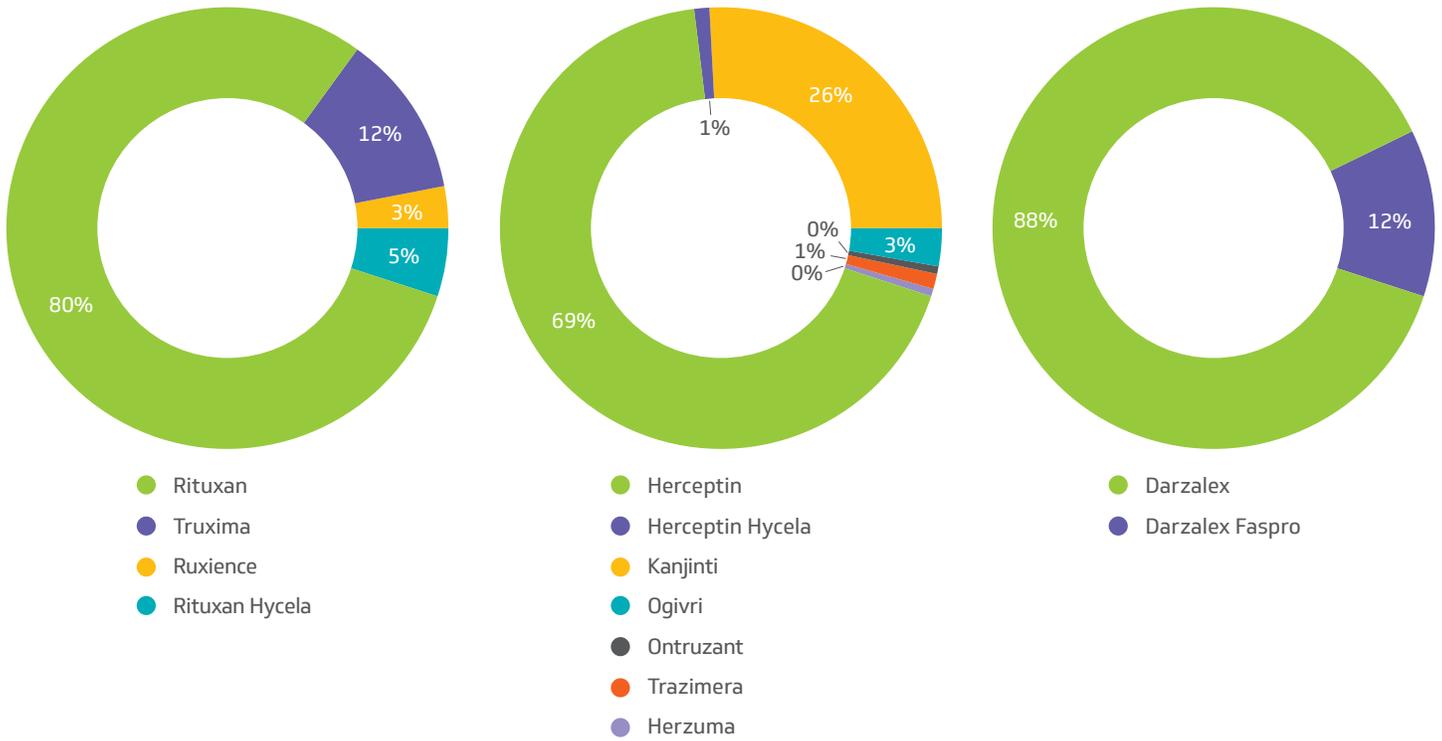
Vizient member data for October 1, 2019–September 30, 2020.
Abbreviation: WAC = wholesale acquisition cost.

New formulations of older products

Subcutaneous administration is a useful alternative to the more common IV route. While subcutaneous formulations of some products have been used in Europe since 2013, they only began to be available in the US market in 2017. The first such product approved was rituximab/hyaluronidase injection (Rituxan Hycela; Genentech), followed by trastuzumab/hyaluronidase injection (Herceptin Hylecta; Genentech). Earlier this year, daratumumab/hyaluronidase injection (Darzalex Faspro; Janssen) was introduced; as of September, it already

accounts for the largest share of market uptake — approximately 12%. Rituximab/hyaluronidase and trastuzumab/hyaluronidase account for approximately 5% and 1% of their respective markets (Figure 2). The lower acceptance of the latter two products may be due to the existence of biosimilar equivalents for their original IV formulations. Formulation changes for older products will continue to influence the market, as products that require lower volumes and less time for administration both improve patients' quality of life and provide operational benefits.

Figure 2. Market shares of rituxan, herceptin, and darzalex products



Data from IQVIA for January to September 2020.³

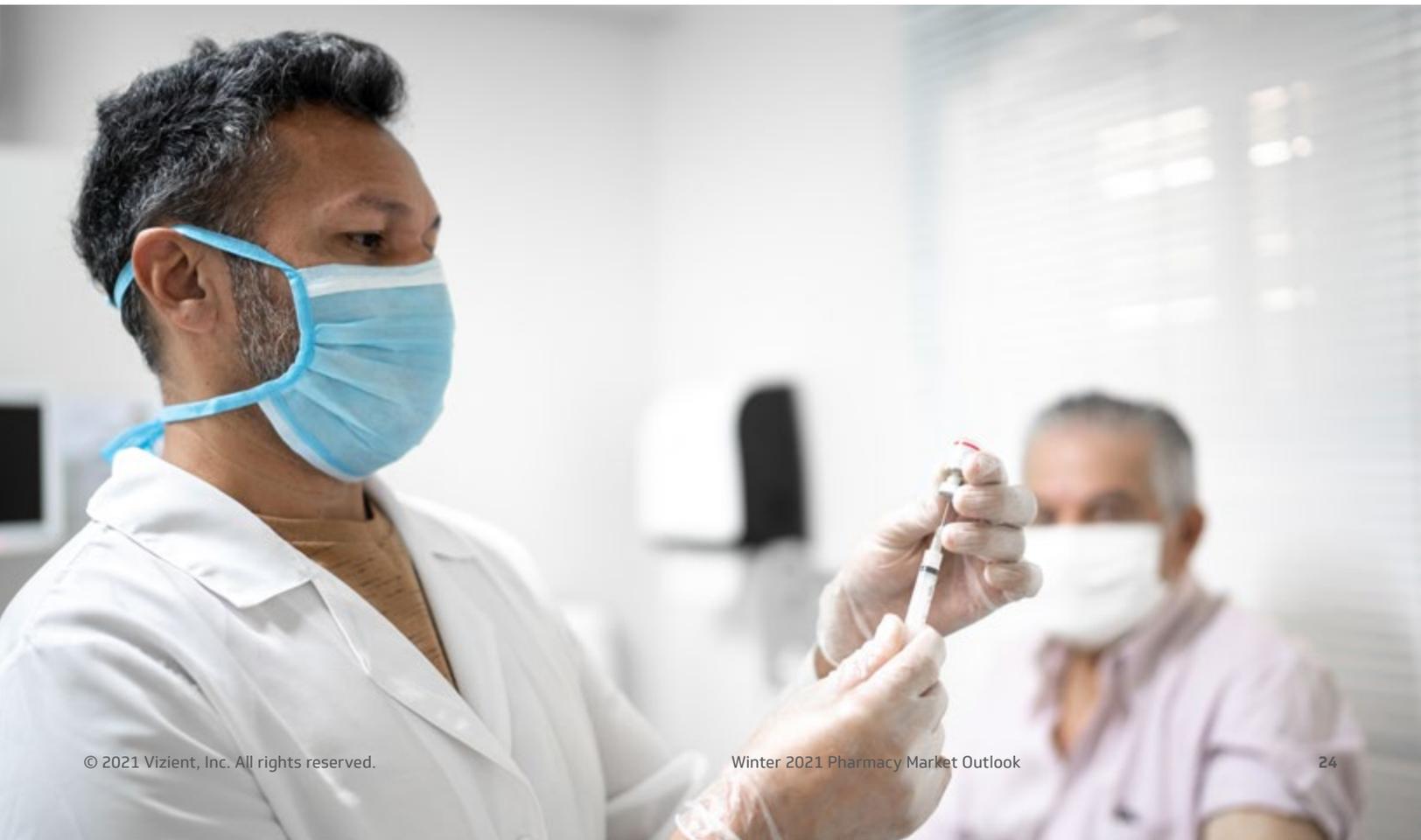


Table 14. Oncology drugs entering the market in 2021

Drug	Manufacturer	Mechanism of action	Indication	PDUFA date
Dostarlimab	GlaxoSmithKline	Anti-PD-1 monoclonal antibody	Recurrent endometrial cancer	Jan 14, 2021
Tepotinib	Merck	MET inhibitor	NSCLC	Feb 25, 2021
Melflufen (melphalan flufenamide)	Oncopeptides AB	Drug conjugate	Refractory multiple myeloma	Feb 28, 2021
Paclitaxel and encephalid	Athenex	Oral formulation of paclitaxel	Metastatic breast cancer	Feb 28, 2021
Idecabtagene vicleucel	Bristol Myers Squibb/ Bluebird Bio	CAR T-cell agent	Multiple myeloma	Mar 27, 2021
Tivozanib	Aveo Oncology	TKI	Renal cell carcinoma	Mar 31, 2021
131I-omburtamab (Omblastys)	Y-mAbs Therapeutics	Radiolabeled monoclonal antibody	Pediatric neuroblastoma	Apr 5, 2021
Leuprolide mesylate depot	Foresee Pharmaceuticals	6-month injectable	Advanced prostate cancer	May 27, 2021
Umbralisib	TG Therapeutics	PI3K and CK1 inhibitor	Follicular lymphoma	Jun 15, 2021
Belumosudil	Kadmon	Rho kinase inhibitor	Graft-vs-host disease	Q3 2021
Loncastuximab tesirine	ADC Therapeutics	Antibody-drug conjugate CD19-directed agent	Diffuse large B-cell lymphoma	Sep 21, 2021

Abbreviations: CAR = chimeric antigen receptor; CK1 = casein kinase 1; NSCLC = non-small-cell lung cancer; PI3K = phosphoinositide-3 kinase; PDUFA = Prescription Drug User Fee Act; TKI = tyrosine kinase inhibitor.

Continued innovation

Despite the ongoing pandemic, the FDA has continued to approve new molecular entities and additional indications for existing oncology agents. In 2019, the FDA approved a record 18 new molecular entities; in comparison, 16 new molecular entities had been approved as of November 2020, and the FDA was expected to surpass its 2019 record by the end of 2020.

Pipeline

The oncology drug pipeline for 2021 is expected to provide a plethora of specialty drugs with orphan designations. Table 14 displays products expected to come to the market in 2021.

Many oncology medications are expected to receive approval for additional indications in 2021: axicabtagene ciloleucel (Yescarta; Kite Pharma), pembrolizumab, selinexor

(Kyprolis; Amgen), cabozantinib (Cabometyx; Exelixis), nivolumab, ipilimumab (Yervoy; Bristol Myers Squibb), and pralsetinib (Gavreto; Blueprint/Genentech). New indications will span a range of oncology disease states, increasing upfront usage of certain agents. Pembrolizumab is expected to receive an indication for triple-negative breast cancer in combination with chemotherapy. Selinexor is projected to be granted approval as an earlier line of therapy for adults with multiple myeloma.

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Infectious disease

2.70%

Period projected
inflation rate

11.23%

Portion of drug spend

The infectious diseases segment continues to be an area to watch, especially given the impact of the COVID-19 pandemic. A comparison of spend on anti-infectives for the third quarter of 2020 shows an overall 20.1% decrease compared with the same period in 2019. Spend on antibiotics in the acute care setting has also shifted over the last year. Vancomycin, daptomycin, posaconazole, ertapenem, and ceftazidime/avibactam are still among the 10 highest-spend antibacterials and antifungals but now account for smaller shares of that segment, while spend for rifaximin, amphotericin B liposome, piperacillin/tazobactam, and micafungin has grown (Table 15). The changes may be the result of differences in price, quantity purchased, or a combination.

Table 15. Acute care antibiotic and antimicrobial spend

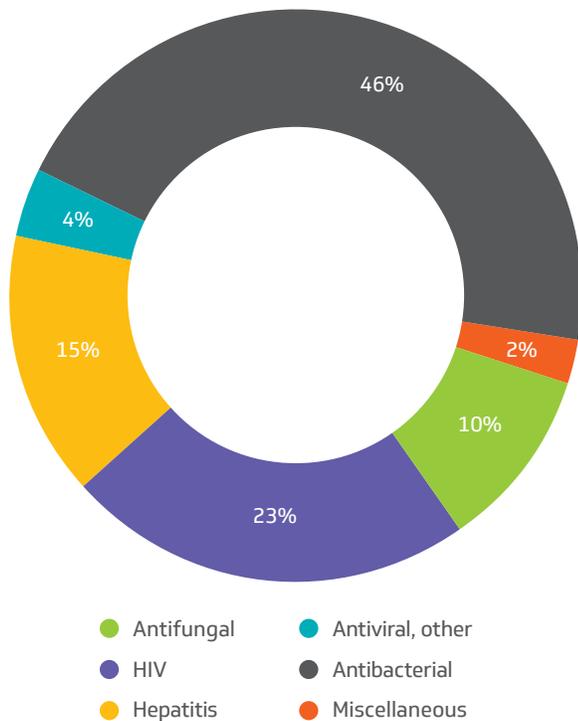
Drug name	Percentage of member spend	Change from 2019 forecast period, % ^a	
		Units purchased	Spend
Vancomycin HCl	6.2	-17.8	-23.8
Rifaximin	6.0	-7.5	-3.5
Daptomycin	5.6	-18.3	-55.5
Amphotericin B liposome	4.7	-15.0	-8.1
Posaconazole	4.3	3.4	-33.4
Ceftaroline fosamil acetate	4.2	-12.8	-6.9
Piperacillin sodium/tazobactam sodium	3.8	-13.1	-21.6
Ertapenem sodium	3.8	-14.5	-35.2
Micafungin sodium	3.6	-4.4	1.7
Ceftazidime/avibactam sodium	2.9	-32.7	-32.4

Vizient member data for October 1, 2019-September 30, 2020.

^a Comparison period: October 1, 2018-September 30, 2019.

The breakdown of total infectious disease-related spend excluding vaccines is consistent with previous Vizient forecasts (Figure 3).

Figure 3. Total infectious diseases spend excluding vaccines, all classes of trade



Vizient member data for October 1, 2019–September 30, 2020.

Influenza

While attention has recently focused on the COVID-19 pandemic, influenza remains a formidable disease. One long-standing workhorse agent for influenza is oseltamivir (Tamiflu; Genentech), which can be used in adult and pediatric patients for treatment or prophylaxis. Purchase volumes for oseltamivir increased by 226% for the third quarter of 2020 compared with the same period in 2019, likely as a result of anticipatory purchasing to hedge against a COVID-19 and influenza “twindemic” and the mass distribution of 200,000 preemptive kits including a course of oseltamivir to at-risk Medicare patients¹; the largest increases occurred in the acute care and ambulatory care settings. While the approach of proactively supplying antiviral influenza medication to well patients prior to infection is innovative (especially during a pandemic, when resources are limited) and may improve time to first dose for some eligible patients, there are legitimate concerns about this practice, including medication safety, waste stream and resistance implications.

Vancomycin guidelines

Revised vancomycin guidelines² for the treatment of methicillin-resistant *Staphylococcus aureus* infections were released in March 2020. During a June 2020 webinar reviewing these guidelines, Vizient conducted a live poll of participating attendees to gauge members’ uptake of an area-under-the-curve (AUC) approach as recommended in the guidelines. At that time, the majority of attendees had not transitioned to an AUC method for either adult or pediatric patients (Table 16). Poll results may have been biased by the subject matter of the program (i.e., members that were already using AUC dosing may not have attended) and it is expected that adherence to the guidelines will increase with time, although acceptance and application are not universal.³

Table 16. Pharmacokinetic approaches to monitoring and adjusting dosing among Vizient members

Approach	Percentage of patients for whom approach is used	
	Adult	Pediatric
Trough-based	78	69
AUC (Bayesian)	5	0
AUC (trapezoidal)	4	0
Other	2	5
Unknown	2	10
None	0	10

Data derived from live poll of Vizient member webinar attendees, June 18, 2020. Abbreviation: AUC = area under the curve.

Fungal disease and COVID-19

Concerns have been raised about concomitant COVID-19 and fungal infections, specifically aspergillosis and candidiasis.^{4,5} Risks may be influenced by immunocompromised status, either innate or in patients receiving immunosuppressant agents (e.g., dexamethasone) in some COVID-19 patients.⁶⁻⁸ Cases of COVID-19–associated pulmonary aspergillosis and candidiasis in various settings have been reported in the literature.^{5,9,10} While this therapeutic arena is evolving, spend patterns may provide some guidance as to what can be expected. Although total anti-infective purchase volumes decreased by 18.7% in the third quarter of 2020 compared with 2019, acute care caspofungin purchases were up 32.8% for the same time period. An upward trend was also seen for the echinocandins anidulafungin (13.0%) and micafungin (6.2%). While spend on voriconazole and

amphotericin B lipid complex were flat, spend for posaconazole and conventional amphotericin B grew by 17.1% and 16.9%, respectively. A decrease in purchase volume was observed for amphotericin B liposomal (10.2%). Future editions of the Pharmacy Market Outlook may further clarify the clinical significance of and possible treatment approaches for such concomitant infections.

Parenteral tetracyclines

The dynamic injectable tetracycline market, which includes novel and legacy agents (i.e., doxycycline, eravacycline, minocycline, omadacycline, tigecycline), continues to meet a specialized need in the infectious diseases arena. Of particular interest is omadacycline, a tetracycline derivative which was approved by the FDA in October 2018 for community-acquired pneumonia and skin and skin structure infections caused by specific microorganisms.¹¹ Additionally, data published in October 2020 highlighted a potential role for omadacycline in the treatment of *Mycobacterium abscessus* disease.¹² The FDA's list of essential medicines, published in August 2020, designated omadacycline as important for the treatment of biological threats, presumably *Bacillus anthracis* and *Yersinia pestis*.^{13,14} While overall it does not account for a large portion of acute care antimicrobial spend, omadacycline spend for the third quarter of 2020 increased by 378% compared with the same period in 2019.

Infectious diseases pipeline

The infectious diseases pipeline holds some interesting prospects.¹⁵

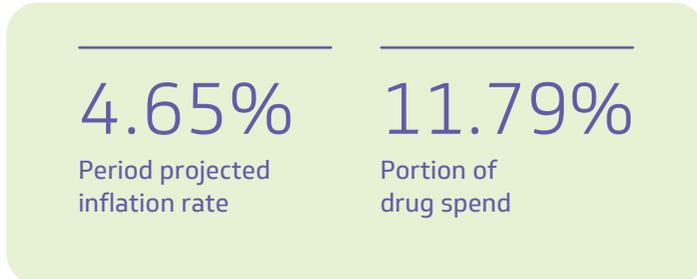
- Sulopenem (Iterum Therapeutics) is a penem antibiotic available as an oral and parenteral formulation which is being evaluated for multiple indications, including complicated intra-abdominal infection and pyelonephritis. Iterum expects to file a new drug application in mid-2021.
- Tebipenem pivoxil hydrobromide (Spero Therapeutics) is an oral carbapenem currently in phase 3 trials for pyelonephritis and multi-drug-resistant urinary tract infection.
- Cefepime-taniborbactam (Venatorx Pharmaceuticals) is a fourth-generation cephalosporin beta-lactamase inhibitor combination also in phase 3 trials for the treatment of urinary tract infection and pyelonephritis.
- Ibrexafungerp citrate (Scynexis) is a semisynthetic enfunafungin derivative (glucan synthase inhibitor) with fungal cell wall activity now in the preregistration phase for treatment of vulvovaginal candidiasis. This oral and parenteral agent is also in phase 3 trials for several other mycotic indications including aspergillosis, blastomycosis, candidiasis, coccidiomycosis, and histoplasmosis.

- Delamanid (Otsuka Pharmaceutical) is an oral nitro-dihydro-imidazooxazole derivative that acts as an antituberculosis agent by targeting the mycobacterium cell wall. It is currently in phase 3 trials for multi-drug-resistant disease when used in an appropriate combination tuberculosis regimen.

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- 2 Rybak MJ, Le J, Lodise TP, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant infections: a revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Disease Pharmacists. *Am J Health Syst Pharm*. 2020;77(11):835-864. doi:10.1093/ajhp/zxaa036
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- 8 Coronavirus-19 (COVID-19) treatment guidelines. National Institutes of Health. Updated November 3, 2020. Accessed November 11, 2020. <https://www.covid19treatmentguidelines.nih.gov>
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Immunomodulators and disease-modifying therapies

Disease-modifying antirheumatic agents



Immunomodulators and disease-modifying therapies



A closer look

The oral multiple sclerosis (MS) drug market has recently seen several new entrants. The biggest splash was the at-risk launch of Mylan's dimethyl fumarate (DMF), a generic version of Biogen's Tecfidera, in August 2020, which was followed by approved abbreviated new drug applications from other DMF manufacturers. It is anticipated that the cost of DMF will decrease rapidly in 2021 as a result of the newly competitive market.

Uptake of the fumarate derivatives — diroximel fumarate (Vumerity; Biogen) and monomethyl fumarate (Bafiertam; Banner Life Sciences) — will also be affected by the DMF launches. These “me-too” follow-on drugs for DMF were approved via the 505(b)(2) pathway based on Tecfidera's clinical trials and bioavailability studies. Both fumarate derivative therapies will compete with DMF for market share, although payers are likely to either restrict their use or classify them as nonformulary drugs.

Payers will also evaluate the newer oral sphingosine 1-phosphate (S1P) receptor modulators, ozanimod (Zeposia; Bristol Myers Squibb) and siponimod (Mayzent; Novartis), against lower-cost alternatives like DMF for formulary inclusion. If legal hurdles are met, the S1P fingolimod (Gilenya; Novartis) may face generic competition in 2021. Fingolimod requires first-dose monitoring for 6 hours in a professional setting for all patients because of the risk of bradycardia; this requirement has led to a loss of market share to the newer S1P receptor modulators. Siponimod has pharmacogenomic metabolism variations. It is contraindicated in patients who are CYP 2C9*3/*3; therefore, manufacturer-covered CYP 2C9 genetic testing is required before starting therapy. Ozanimod, in contrast, does not require genetic testing or cardiac monitoring. However, it does carry precautions about concomitant use with serotonergic medications and tyramine-containing

foods. More information about the S1P receptor modulators can be found in a recent Vizient class review.

According to a list of the 20 most expensive prescription drugs in the US published by GoodRx,¹ cladribine (Mavenclad; Merck KgaA/EMD Serono) ranked second, with a list price of \$56,954 for a single course of therapy. The oral therapy is taken in 2 treatment courses 12 months apart. The price of cladribine had increased by 6% as of April 2020; its use, however, has decreased significantly. The decrease may be due to providers' qualms about prescribing a therapy that temporarily reduces the number of both T and B lymphocytes in the body, possibly suppressing the patient's immune system, during the COVID-19 pandemic.

A new self-injectable drug for the treatment of MS, ofatumumab (Kesimpta, Novartis) was approved in August 2020. Ofatumumab, also approved for the treatment of chronic lymphocytic leukemia, is a recombinant human monoclonal antibody given subcutaneously 3 weeks in a row as a loading dose and monthly thereafter, and is the first at-home, self-administered anti-CD20 therapy. Ofatumumab is expected to give the blockbuster drug ocrelizumab (Ocrevus, Roche/Genentech), which is a twice-yearly infusion, some strong competition. However, providers may be wary about prescribing it for some patients, since the lack of control over administration could result in compliance issues.

Changes in the rheumatoid arthritis (RA) market are largely a result of the availability of biosimilars. Infliximab-axxq (Avsola; Amgen), the biosimilar for Janssen's Remicade, finally launched in June 2020 after being originally approved by the FDA in December 2019. In July 2020, the FDA approved adalimumab-fkjp (Hulio, Fujifilm Kyowa Kirin Biologics/Mylan) injection for subcutaneous use, a biosimilar for Humira (AbbVie). Mylan is expected to launch adalimumab-fkjp in the US in July 2023.

COVID-19

The Multiple Sclerosis International Federation's global COVID-19 advice² supports an individual strategy of clinical management for MS patients during the COVID-19 pandemic. The recommendation is based on emerging evidence that suggests that simply having MS does not make a person more susceptible to COVID-19, more likely to have severe disease, or more likely to die than the general population. However, the following risk factors do make MS patients more susceptible to developing severe illness if they are infected with SARS-CoV-2³:

- Progressive MS
- Age ≥ 60 years
- Male gender
- Black and possibly South Asian race/ethnicity
- Expanded Disability Status Scale score ≥ 6
- Body mass index ≥ 30
- Underlying conditions such as heart or lung disease or diabetes
- Use of disease-modifying therapies (DMTs)

Registry data from clinicians in 21 countries participating in the Global COVID-19 and MS Data Sharing Initiative found that MS patients treated with an anti-CD20 monoclonal antibody had significantly higher risk of hospitalization, ICU admission, and need for mechanical ventilation than patients treated with DMTs with different mechanisms of action.⁴ Patients using ocrelizumab, ofatumumab, or rituximab should be especially careful to follow the CDC guidelines to avoid contracting the virus.⁵ Other infused therapies that require patients to come to a health care facility, such as natalizumab, were not associated with higher risk of severe COVID-19.^{6,7} More studies and larger cohorts are needed to clarify the clinical management of MS patients with DMTs in the context of COVID-19 and the impact of DMTs on antiviral antibody production.⁸

Some DMTs are actually being studied for the treatment of COVID-19. One ongoing phase 3 study, the Adaptive COVID-19 Treatment Trial 3 (ACTT 3), is investigating subcutaneous interferon beta-1a (Rebif; EMD Serono) in combination with remdesivir (Veklury; Gilead) for the treatment of COVID-19 in hospitalized adults.⁹ Another immunomodulator, interferon beta-1b (Betaseron; Bayer), is also being investigated as a component of a 3-drug regimen in multicenter, prospective, open-label, randomized, phase 2 trial in adults with COVID-19 who were admitted to 1 of 6 hospitals in Hong Kong. The other drugs making up the cocktail are the HIV oral combination lopinavir-ritonavir and the antiviral ribavirin.¹⁰

Many RA therapies are being investigated for the treatment of COVID-19. Because anti-tumor necrosis factor (anti-TNF) therapies, such as infliximab and adalimumab, have a track record of decreasing inflammation in RA, they are being investigated to treat COVID-19 patients who develop acute respiratory distress syndrome.

The National Institute of Allergy and Infectious Diseases (NIAID) has launched a trial of remdesivir and baricitinib (Olumiant; Eli Lilly/Incyte) for the treatment of hospitalized COVID-19 patients. Baricitinib is a JAK inhibitor indicated for the treatment of adult patients with moderate to severe active RA who have had an inadequate response to 1 or more TNF antagonist therapies. Baricitinib is also being investigated as a monotherapy for the prevention of cytokine storm associated with COVID-19.

Trials have begun for the use of tocilizumab (Actemra; Roche) in combination with remdesivir in hospitalized patients with severe COVID-19 pneumonia. Tocilizumab is an interleukin-6 (IL-6) receptor antagonist indicated for the treatment of adult patients with moderate to severe RA who have had an inadequate response to 1 or more DMARDs. Tocilizumab monotherapy studies have shown mixed results. The idea behind using IL-6 inhibitors to treat COVID-19 patients is to counter the overreaction of the immune system that causes pneumonia. Another IL-6 inhibitor used for RA that is being studied as a potential treatment for COVID-19 is sarilumab (Kevzara; Regeneron/Sanofi). The RA investigational drug otilimab (GSK 3196165; GlaxoSmithKline), an anti-granulocyte macrophage colony-stimulating factor, is also being studied for the treatment of pneumonia caused by COVID-19.

What's next

Patent disputes are delaying the market entry of approved generic versions of fingolimod and teriflunomide (Aubagio; Sanofi). However, another S1P receptor modulator, ponesimod (ACT-128800; Janssen), may enter an already crowded market in March 2021, providing an additional oral treatment option for patients with relapsing forms of MS. Other MS pipeline drugs that are in phase 3 clinical trials include fenebrutinib (GDC-0853; Genentech), ibudilast (MN-166; MediciNova), and ublituximab (TGTX-1101; TG Therapeutics). Fenebrutinib is an oral dual inhibitor of both B-cell and myeloid lineage-cell activation, which may suppress disease activity and slow disease progression by targeting both acute and chronic inflammatory aspects of MS. Ibudilast is a twice-daily oral nonselective phosphodiesterase inhibitor that may reduce inflammation in the brain. Ublituximab is a glycoengineered anti-CD20 monoclonal antibody expected to offer infusion times of 30 to 60 minutes, compared with the 4-hour infusion time for ocrelizumab.

Filgotinib (Gilead), an investigational treatment for moderately to severely active RA, would have been the fourth oral JAK inhibitor on the market, joining baricitinib (Olumiant; Eli Lilly), tofacitinib (Xeljanz; Pfizer) and upadacitinib (Rinvoq; AbbVie). However, although it was approved in Japan in August 2020, the FDA issued a complete response letter for filgotinib's new drug application. The need for more data moves the potential approval of filgotinib from an anticipated date of late 2020 to early 2022.

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- 4 Global Data Sharing Initiative database. MS International Foundation. Updated July 6, 2020. Accessed November 10, 2020. <https://www.msif.org/covid-19-ms-data-sharing-for-healthcare-professionals>
- 5 Coronavirus disease 2019 (COVID-19): How to protect yourself and others. Centers for Disease Control and Prevention. Updated November 4, 2020. Accessed November 11, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html>
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- 7 Hughes R, Fitovski K, Whitley L, et al. COVID-19 in persons with multiple sclerosis treated with ocrelizumab: pharmacovigilance update. Presented at: MSVirtual2020; September 11-13, 2020. Abstract S502.05
- 8 Iannetta M, Cesta N, Stingone C, et al. Mild clinical manifestations of SARS-CoV-2 related pneumonia in two patients with multiple sclerosis under treatment with ocrelizumab. *Mult Scler Relat Disord.* 2020;45:102442. doi:10.1016/j.msard.2020.102442
- 9 Adaptive COVID-19 treatment trial 3. ClinicalTrials.gov. Updated November 13, 2020. Accessed November 10, 2020. <https://clinicaltrials.gov/ct2/show/NCT04492475>
- 10 Hung IF, Lung KC, Tso EY, et al. Triple combination of interferon beta-1b, lopinavir-ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial. *Lancet.* 2020;395(10238):1695-1704.



Plasma critical care products: IgIV and albumin

3.10%

Period projected
inflation rate

4.25%

Portion of drug spend

The COVID-19 pandemic has significant ramifications for the plasma supply chain that are expected to affect the overall market outlook for IV immunoglobulin in 2021, primarily due to the impact on plasma donations. The market outlook for albumin and other plasma-derived products remains relatively stable. Reductions in plasma donations resulting from stay-at-home orders and public concerns about SARS-CoV-2 exposure were noted as early as the second quarter of 2020. As a result, supply is expected to tighten by the first quarter of 2021 and may remain tight into 2022 because of the long manufacturing cycle for plasma products, particularly if the impact on plasma collection and donations is prolonged or recurrent.

Manufacturers have established mitigation strategies in response to supply concerns, including significant investments in plasma collection, and they continue to invest in manufacturing capabilities and infrastructure. Additionally, the favorable reimbursement structure in the US market may position the country to benefit as suppliers review strategies for global supply allocation. However, market tightness and increased manufacturing costs are expected to increase pricing pressures for IgIV throughout 2021. Volume-weighted average pricing for albumin continues to remain stable since large fluctuations in supply are unlikely, although usage has increased somewhat as a result of the COVID-19 pandemic.¹

Clinical trials for COVID-19 immune globulin therapies are ongoing. Convalescent plasma remains an investigational therapy; the FDA has issued guidelines for its use in the treatment of COVID-19.² Manufacturers also continue to work on high-concentration antibody therapies through supplier collaborations and coordination with government agencies (the FDA, National Institutes of Health, and Biomedical Advanced Research and Development Authority) to develop an anti-SARS-CoV-2 hyperimmune globulin.

Vizient continues to assess the market outlook for plasma products and the impact of current research on future supply and demand, particularly with regard to any last effects of COVID-19 on the supply chain and health care system.

- 1 Huang J, Cheng A, Kumar R, et al. Hypoalbuminemia predicts the outcome of COVID-19 independent of age and co-morbidity. *J Med Virol*. 2020;92(10):2152-2158. doi:10.1002/jmv.26003
- 2 Recommendations for investigational COVID-19 convalescent plasma. Food and Drug Administration. November 16, 2020. Accessed December 7, 2020. <https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma>

Hot topics

Vaccine trends: the impact of COVID-19 on the vaccine market

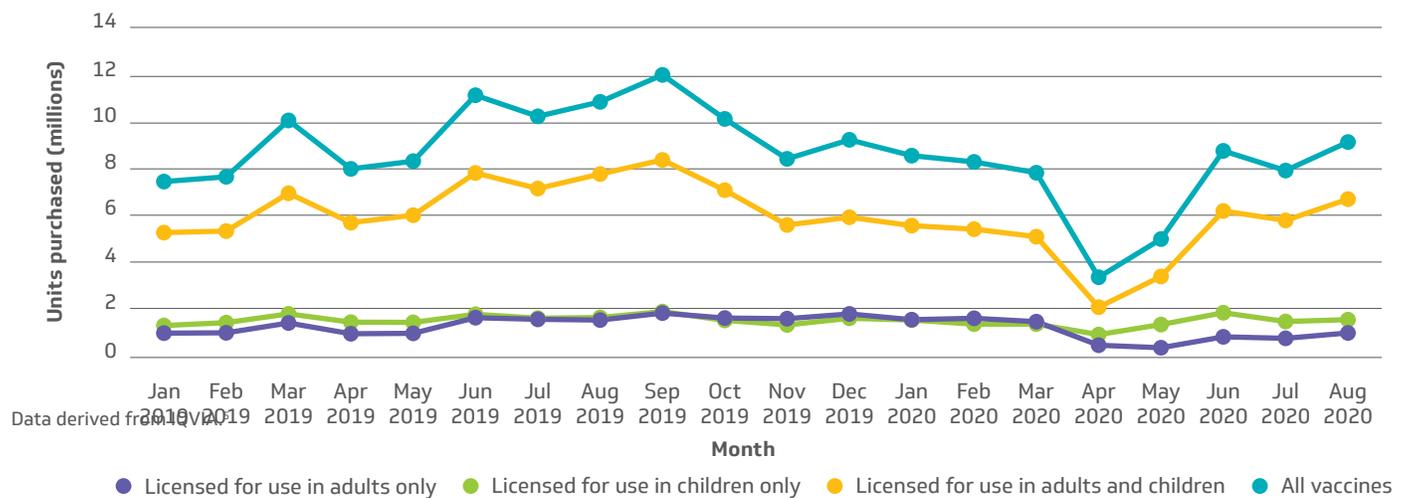
The first case of COVID-19 was reported in the United States on January 20, 2020. By March 13, the virus had reached all 50 states. A national emergency was declared and many states implemented shelter-in-place or stay-at-home orders.¹ As anticipated, this resulted in disruptions to routine preventative and nonemergency care, including routine vaccination. In the March 25 *Immunization Works Newsletter*, the CDC acknowledged these hurdles and encouraged health care practices that were limiting well-child visits to “prioritize newborn care and vaccination of infants and young children (through 24 months of age) when possible.”²

Using multiple data sources, the CDC later examined rates of administration of noninfluenza childhood vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) for January through April 2020 compared with the average vaccination rates for the same period in years past.^{1,3} There was a notable decrease in pediatric (age 0-18 years) vaccination rates beginning the week after the national emergency was declared; however, there was less decline for children aged 0-24 months than for older

children. Similarly, the Clinical Practice Solutions Center® — jointly developed by the Association of American Medical Colleges and Vizient — found 60% fewer pediatric vaccination visits in April 2020 compared with April 2019, based on CPT codes for vaccination visits.⁴

In an effort to examine differences in impact between children and adults, we used IQVIA’s SMART database to examine the “eaches” — i.e., the number of vaccines purchased, with no restriction on setting or class of trade — for all routine ACIP-recommended noninfluenza vaccines purchased from January 2019 to August 2020.⁵ Vaccines were sorted into 3 categories: vaccines licensed for administration to adults only, to children only, and to both populations. The IQVIA data showed a sharp decline in the number of vaccines purchased between March and April 2020. However, by May, vaccine purchases had begun to increase, although volumes remained much lower in the same period of 2019 (Figure 4). The majority of vaccines sold were in the third category — licensed for use in both adults and children — which makes it hard to distinguish the impact on vaccination in either age group.

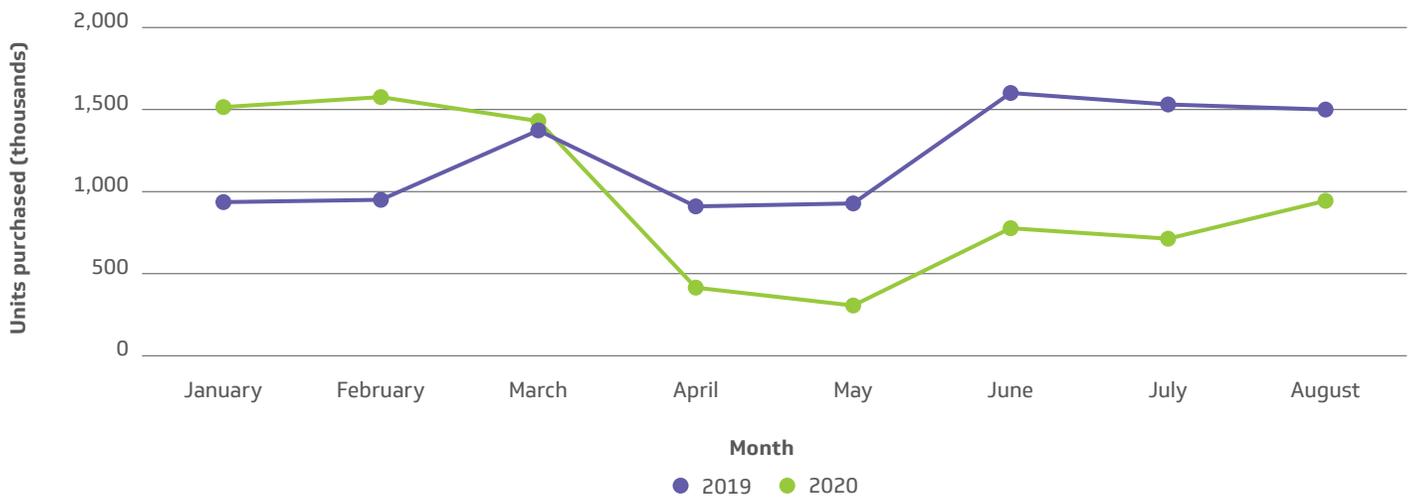
Figure 4. Vaccine purchases by population



Comparing sales of vaccines licensed for use only in adults or only in children for 2019 and 2020 shows that there was a much larger decline for the former. Although vaccine sales were higher across the board at the start of 2020, eaches for vaccines licensed for use in adults plummeted in April and have been slow to recover (Figure 5). Purchases of vaccines only licensed for use in pediatric patients decreased in April but were already back to levels seen in 2019 by May 2020 (Figure 6).

The apparent difference in recovery rates for adult and pediatric vaccine sales may be due in part to the emphasis placed on the importance of well-child visits and vaccinations, especially in the 0-24 month age group. However, this data should serve as a reminder of the importance of routine vaccination for all age groups.

Figure 5. Purchases of vaccines licensed for use in adults only, 2019 vs 2020



Data derived from IQVIA.⁵

Figure 6. Purchases of vaccines licensed for use in pediatric patients only, 2019 vs 2020



Data derived from IQVIA.⁵

Pharmacy staff as COVID-19 vaccine administrators

There will likely be a role for pharmacists and pharmacy technicians and interns to play as COVID-19 vaccine administrators, since pharmacists are the most accessible health care professionals and national resources continue to be strained. In October, the Department of Health and Human Services announced approval for qualified pharmacy technicians and state-authorized interns to administer childhood and COVID-19 vaccinations in addition to COVID-19 tests, with specific requirements for each.⁶ Members should refer to their state health departments and boards of pharmacy for additional guidance.

Novel vaccine administration sites of care

Individual states will oversee their own planning for mass COVID-19 vaccination with direction from the federal government. Novel sites of care, such as drive-through clinics, may be leveraged to increase the efficiency and potentially the safety of vaccine administration. This approach has been used for influenza vaccination during the pandemic.

- 1 Santoli JM, Lindley MC, DeSilva MB, et al. Effects of the COVID-19 pandemic on routine pediatric vaccine ordering and administration — United States, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(19):591-593. doi:10.15585/mmwr.mm6919e2
- 2 Centers for Disease Control and Prevention. Maintaining childhood vaccinations during COVID-19 pandemic. *Immunization Works.* March 25, 2020. Accessed November 5, 2020. <https://www.cdc.gov/vaccines/news/newsletters/imwrks/2020/2020-03.html>
- 3 Bramer CA, Kimmins LM, Swanson R, et al. Decline in child vaccination coverage during the COVID-19 pandemic — Michigan Care Improvement Registry, May 2016–May 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(20):630-631. doi:10.15585/mmwr.mm6920e1
- 4 Data insights brief: COVID-19 impact on pediatric vaccination visits. Clinical Practice Solutions Center. Updated July 7, 2020. Accessed November 3, 2020. <https://www.vizientinc.com/our-solutions/supply-chain-solutions/member-programs/-/media/2cbb681557f7495886063bdaf34f50ee.ashx>
- 5 IQVIA SMART Solutions database. IQVIA; 2020. Accessed October 28, 2020. <http://www.iqvia.com>
- 6 Trump administration takes action to further expand access to vaccines, COVID-19 tests. News release. Department of Health and Human Services; October 21, 2020. Accessed November 11, 2020. <https://www.hhs.gov/about/news/2020/10/21/trump-administration-takes-action-further-expand-access-vaccines-covid-19-tests.html>



Biosimilars: almost there?

Given the urgency of the COVID-19 pandemic, it feels like we have been waiting for a vaccine for an excruciatingly long time, in spite of the fact that progress has been historically rapid. Another area in which progress seems to be taking forever is the biosimilars market. Biosimilars have now been available in the US for 10 years, yet the feeling that we have not fully realized the value of these medications persists. However, a recent report shows that biosimilars are delivering on their promises: lower-cost alternatives that expand access to critically important biologic drugs. And as we move out from under the shadow of COVID-19, we are finally nearing the largest biosimilar opportunity that still remains — competitors for adalimumab.

Breadth and depth of competition

As of December 31, the FDA had approved 29 biosimilars (Table 17).¹ Of these, 9 are not yet being marketed because of patent settlements or other business decisions. Still, the increasing number of competitors is putting pressure on prices and enabling expanded adoption of biosimilars.

A recent national analysis estimates that the availability of biosimilars resulted in cost savings for the US market of \$18 billion between 2010 and 2014 and \$19 billion between 2015 and 2019.² However, the greatest savings are projected to occur in the next 5 years²: Between 2020 and 2024, it is estimated that biosimilar availability and use may result in savings of \$104 billion, driven largely by biosimilars for adalimumab that are expected in 2023.² In addition, molecule-specific national sales estimates show trends similar to those for trastuzumab biosimilars.

Table 17. FDA-approved biosimilars as of December 31, 2020

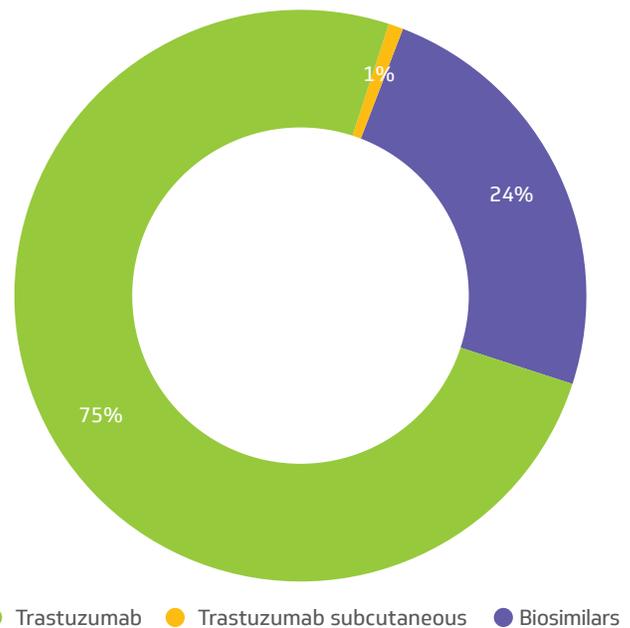
Originator	Approved biosimilars					
	1st	2nd	3rd	4th	5th	6th
Filgrastim	sndz	aafi				
Infliximab	dyyb	abda	qbtx	axxq		
Etanercept	szzs	ykro				
Adalimumab	atto	adbm	adaz	bwwd	afzb	fkjp
Bevacizumab	awwb	brzr				
Trastuzumab	dkst	pkrb	dttb	qyyp	anns	
Epoetin alfa	epbx					
Pegfilgrastim	jmdb	cbqv	bmez	apgf		
Rituximab	abbs	pvvr	arrx			

Drugs in **boldface** are currently on the market.

Trastuzumab biosimilars in action

To date, the FDA has approved 5 biosimilar versions of trastuzumab, all of which had entered the market as of June 2020.³ National data for October 2019 to September 2020 show that these biosimilars accounted for almost a quarter of trastuzumab spend (Figure 7).³

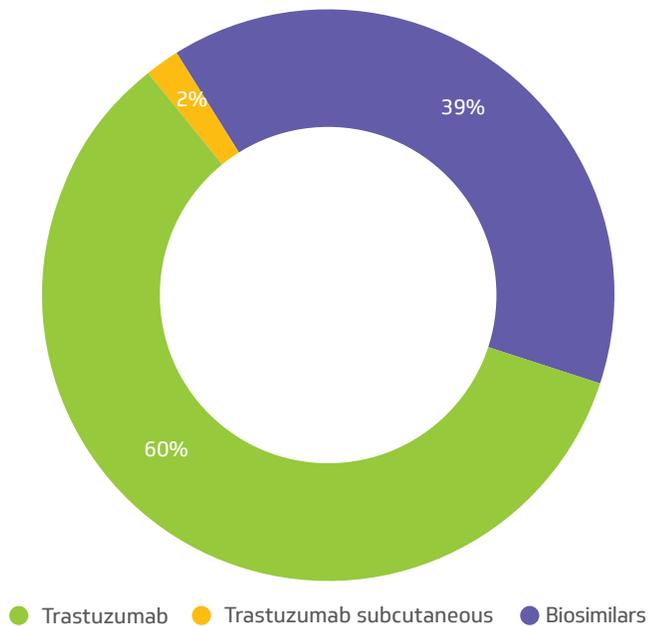
Figure 7. National market share for trastuzumab and its biosimilars, October 2019–September 2020



Data from IQVIA.³ Rounded to nearest whole number.

However, data for September 2020 only — i.e., the most recent month with maximum competition — shows that biosimilars account for almost 40% of spend (Figure 8).³

Figure 8. National market share for trastuzumab and its biosimilars, September 2020



Data from IQVIA.³ Rounded to nearest whole number.

This finding suggests that as the number of competitors continues to grow, biosimilars are gaining greater acceptance. The same trends hold for other products such as biosimilars for rituximab and bevacizumab.³

By the end of the first quarter of 2021, we may see an additional competitors approved for bevacizumab, rituximab, and pegfilgrastim.⁴ However, the target of greatest interest remains adalimumab, for which biosimilars will be launched in 2023.² Sales of adalimumab in the US are approaching \$24 billion,³ and we are currently predicting a price increase of 7.5% over the next 18 months. We anticipate that price increases will continue until the patent settlements expire. These trends, compounded by the COVID-19 pandemic, have created even greater need for cost savings for patients and health care organizations. Therefore, providers must press forward with adoption of biosimilars.

Legal issues to watch

No discussion of biosimilars would be complete without some attention to the legal controversies. The FDA was granted authority to approve biosimilars as part of the

Affordable Care Act (ACA). On November 10, the Supreme Court heard the most recent challenge to the ACA, which seeks to strike down the entire act, arguing that the elimination of the individual mandate in 2017 renders the ACA unconstitutional.⁵ If the challenge succeeds, the FDA's authority to approve biosimilars will cease to exist. However, the Supreme Court may not render a decision until June, and since there is bipartisan support for addressing high drug costs, it is likely that a biosimilar pathway independent of the ACA would be established. Still, this issue illustrates the importance of continued vigilance with regard to legislative, judicial, and regulatory topics.

Preparing for expanding biosimilar availability

Health care providers preparing for increased and expanded biosimilar adoption must plan to meet needs in several areas:

- **Education:** While some may feel extremely familiar with the biosimilar paradigm, others, including prescribers, may still lack understanding. Given the interest in cost savings as the health care industry begins to recover from the COVID-19 pandemic, now is a great time to increase awareness of biosimilars and provide refreshers. Vizient offers sample presentations, examples of member policies, and a value analysis calculator on the [biosimilars resource page](#). It is also important to engage clinicians whose acceptance of biosimilars has been limited (such as gastroenterologists) and those who will soon have the option available to them for the first time (e.g., endocrinologists).
- **Reimbursement:** The most frequent challenge reported to us is the additional work required by and confusion associated with payer formulary decisions that may or may not align with the health system's formulary choices. It is essential for pharmacy organizations to work closely with their finance departments and those who manage relationships with payers, both to correct denials and to promote proactive actions to ensure alignment of coverage. Pharmacy departments at several Vizient member organizations have begun to provide their financial colleagues with language to include in payer negotiations to secure biosimilar coverage at parity with the originator drug or with other biosimilars.
- **Advocacy:** Many legislative, regulatory, and judicial actions could affect the introduction of biosimilars. Pharmacists must remain aware of these potential actions and how they might affect the continued adoption and expansion of biosimilars.

- **Operations:** It is important to implement order pathways that ease or promote the ordering of biosimilars for clinicians and therapeutic substitution policies that allow a pharmacist to switch orders from an originator to a biosimilar when required by an insurance company.

- 1 Biosimilar product information: FDA-approved biosimilar products. Food and Drug Administration. Updated July 7, 2020. Accessed December 30, 2020. <https://www.fda.gov/drugs/biosimilars/biosimilar-product-information>
- 2 The IQVIA Institute. Biosimilars in the *United States 2020-2024: Competition, Savings and Sustainability*. IQVIA. September 29, 2020. Accessed November

10, 2020. <https://www.iqvia.com/insights/the-iqvia-institute/reports/biosimilars-in-the-united-states-2020-2024>

- 3 IQVIA SMART Solutions database. IQVIA; 2020. Accessed November 10, 2020. <https://www.iqvia.com/locations/united-states/solutions/business-intelligence-and-analytics/smart-syndicated-data>
- 4 FDA performance tracker: biosimilars. The Pink Sheet. Informa PharmaIntelligence. Accessed November 10, 2020. <https://pink.pharmaintelligence.informa.com/datasets/review-pathways/biosimilars>
- 5 Hagen T. Supreme Court hints biosimilar route might be preserved. Center for Biosimilars. November 10, 2020. Accessed November 10, 2020. <https://www.centerforbiosimilars.com/view/supreme-court-hints-biosimilar-route-might-be-preserved>

Regulatory updates

Drug Supply Chain Security Act

Just weeks before the November 2020 enforcement deadline for certain provisions of the Drug Supply Chain Security Act (DSCSA), the FDA announced a delay. According to guidance, enforcement discretion will be given until November 2023 for the requirement that dispensers investigate product identifiers on suspect and illegitimate product and that distributors verify product identifiers on saleable returned product.¹

The requirement that dispensers only buy and sell products with a product identifier on the package was not delayed and therefore went into effect on November 27. Drugs manufactured after November 27, 2018, must be affixed or imprinted with a product identifier that features the product's NDC plus a unique serial number, lot number, and an expiration date; dispensers should have processes in place to ensure that the product identifier is on the package when they receive products that require it. Products that are not required to include product identifiers include blood or blood components intended for transfusion, certain radioactive drugs and radioactive biological products, imaging drugs, certain intravenous products, medical gases, homeopathic drugs, and drugs compounded in compliance with sections 503A or 503B of the Food, Drug, and Cosmetic Act.

Dispensers should continue to actively prepare for DSCSA compliance, by first ensuring that they are compliant with current dispenser requirements. Several organizations have provided resources and guidance:

- The Pharmaceutical Distribution Security Alliance has published a resource on current dispenser requirements.²
- The GS1 US Implementation Guideline: Applying GS1 Standards for DSCSA and Traceability Release 1.2 describes implementation of GS1 standards, including

the GS1 Electronic Product Code Information Services, to support DSCSA lot-level management, serialization, and item-level traceability.³

- The Healthcare Distribution Alliance's position statement, *Enhanced Drug Distribution Security Traceability in 2023 and Beyond*, contains a detailed explanation of 2023 DSCSA requirements and how they apply to the supply chain.⁴

In addition, the Vizient DSCSA webpage provides a side-by-side comparison of the features of the DSCSA solution offerings from third-party providers and wholesale distributors to help members make an informed selection of a DSCSA solution provider.

Drug importation

The Safe Importation Action Plan final rule went into effect on November 30.⁵ This rule implements a provision of federal law that allows FDA-authorized programs to import certain prescription drugs from Canada under specific conditions to ensure that the importation poses no additional risk to the public's health and safety and significantly reduces the cost of covered products for the American consumer. Several states have enacted laws establishing drug importation programs and supporting a requirement that proposed programs be submitted to the FDA for approval.

The final guidance for industry describes procedures drug manufacturers can follow to facilitate importation of prescription drugs, including biological products, that are approved by the FDA, manufactured abroad, authorized for sale in any foreign country, and originally intended for sale in that foreign country.⁶

Pharmaceutical compounding

Four new bulk substances have been recommended by the FDA for inclusion on the list of active pharmaceutical ingredients that outsourcing facilities can use in drug compounding under section 503B of the Food, Drug, and Cosmetic Act⁷: diphenylcyclopropanone, glycolic acid, squaric acid dibutyl ester, and trichloroacetic acid.

Another 19 bulk drug substances were considered for inclusion, but based on the information reviewed, the agency did not find that the statutory standard — a clinical need for an outsourcing facility to compound drug products starting from these bulk drug substances — had been met. The 19 substances not proposed for inclusion are diazepam, dobutamine HCl, dopamine HCl, edetate calcium disodium, folic acid, glycopyrrolate, hydroxyzine HCl, ketorolac tromethamine, labetalol HCl, mannitol, metoclopramide HCl, moxifloxacin HCl, nalbuphine HCl, polidocanol, potassium acetate, procainamide HCl, sodium nitroprusside, sodium thiosulfate, and verapamil HCl.⁸ The FDA is seeking public comment on this proposal before finalizing its decision.

Continuing its efforts to protect patients from exposure to poor-quality compounded drugs, the FDA has recently published 2 final guidances for industry. The first, a standard memorandum of understanding (MOU) between the FDA and the state boards of pharmacy,⁹ is a key public health protection in the Drug Quality and Security Act and addresses certain interstate distributions of compounded drugs by traditional compounders (i.e., 503A pharmacies). State regulators are to investigate complaints about adverse drug experiences and product quality issues involving drugs that are compounded at pharmacies within the state and distributed outside the state. State regulators will also have an efficient information-sharing channel they can use to advise the FDA when they receive reports of serious adverse drug experiences or product quality issues, such as contamination, related to compounded drugs. This channel is expected to facilitate early collaboration on issues that have the potential to affect patients in multiple states.

Once signed by states, the MOU will serve as an important mechanism for sharing information about compounders, primarily pharmacies, that distribute compounded drugs across state lines. The law (section 503A of the Federal Food, Drug, and Cosmetic Act) limits distribution of compounded drugs outside the state by a pharmacist, pharmacy, or physician located in a state that has not signed on the MOU to 5% of its total prescription orders dispensed or distributed. To provide ample time for state review, the FDA has increased the amount of time available for signature from 180 days to 365 days before the 5%

limit will be enforced in states that have not signed the final MOU. This extended time frame should correspond to a full legislative cycle for most states, allowing them time to modify their laws and regulations if necessary.

The second guidance document, “Insanitary Conditions at Compounding Facilities: Guidance for Industry,” provides recent examples of insanitary conditions that FDA has observed at compounding facilities and details corrective actions that facilities should take when they identify these conditions.¹⁰ The final guidance is largely the same as the draft guidance, with minor clarifications regarding processing beta-lactams, the handling of radiopharmaceuticals, and physician compounding and repackaging activities. The most significant alteration in the final guidance is a change in a risk management approach to prevent the occurrence of insanitary conditions. The FDA recommends that compounders use risk management tools to develop appropriate controls to prevent insanitary conditions at facilities. The guidance also addresses the regulatory actions that FDA may take in response to these conditions. Despite the exemptions, compounders are still required to abide by section 501(a)(2)(A) of the Food, Drug, and Cosmetic Act, which states that a drug is adulterated “if it has been prepared, packaged, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health.”¹⁰

Donning appropriate PPE during compounding is a requirement under the previous final guidance. However, shortages of gowns, masks, and shoe covers resulting from the surge in demand during the COVID-19 pandemic continue to plague pharmacy departments, which also need PPE for drug compounding and hazardous drug handling. Supplies of PPE will also be needed for COVID-19 vaccine administration. The Department of Health and Human Services recently announced plans to provide ancillary supply kits containing needles, syringes, alcohol prep pads, surgical masks, and face shields to health care workers who will be administering COVID-19 vaccines.¹¹ Each kit will contain enough supplies to administer up to 100 doses of vaccine. However, the kits will not include sharps containers, gloves, or bandages, or any PPE specifically required by the provider site. Currently, PPE suppliers are still experiencing increased demand while coping with reduced global production capacity and substantial labor and packaging cost increases. These higher costs are being passed on to product purchasers.

The USP Appeals Panel recently issued decisions on the appeals to USP General Chapters <795>, <797>, and <825>.¹² The appeals to the revised chapters <795> and <797>, dealing with nonsterile and sterile compounding,

were granted, and the revisions will go back to the Compounding Expert Committee with the recommendation for further engagement on the issues concerning the beyond-use date provisions. As a part of the stakeholder engagement plan,¹³ USP held an open forum for beyond-use date provisions in General Chapter <795> and <797> on September 15, 2020.¹⁴ The revision, comment, and review processes are currently under way.

The appeal to new USP chapter <825>, on radiopharmaceutical compounding, was denied. Following the resolution of the appeal, the USP Chemical Medicines 4 Expert Committee established a new official date of December 1, 2020, which provided a 6-month implementation period. However, the chapter is informational, unless otherwise required by a regulatory body.¹⁵

Hazardous drugs

USP chapter <800>, on safe handling of hazardous drugs, was not subject to appeal and became official on December 1, 2019. Like chapter <825>, chapter <800> remains informational and not compendially applicable until the revised USP chapters <795> and <797>, which refer to chapter <800>, become official.¹⁶ USP encourages application of chapter <800> in the interest of advancing public health, and regulators may make their own determinations regarding its enforceability. The Occupational Safety and Health Administration, National Institute for Occupational Safety and Health (NIOSH), and the Environmental Protection Agency (EPA) currently have enforceable federal regulations related to hazardous drug handling and exposure.

NIOSH released a draft of its 2020 List of Hazardous Drugs in Healthcare Settings in May.¹⁷ The draft proposed a reorganization of the tables in a manner that may address at least some concerns that have been expressed. For example, NIOSH determined that grouping all antineoplastic drugs together in one table is no longer the most useful or informative method for the user. Proposed changes to the list structure would remove Table 3 and place all drugs in either Table 1 or Table 2:

- Table 1: Drugs that contain manufacturer's special handling information (MSHI) in the package insert and/or meet the NIOSH definition of a hazardous drug and are classified by the National Toxicology Program (NTP) as "known to be a human carcinogen," or by the International Agency for Research on Cancer (IARC) as "carcinogenic" or "probably carcinogenic."
- Table 2: Drugs that meet the NIOSH definition of a hazardous drug but do not have MSHI and are not classified by NTP as "known to be a human carcinogen," or by IARC as "carcinogenic" or "probably carcinogenic."

The Joint Commission clarified that its medication compounding surveys will be based on the 2008 version of USP chapter <797>.¹⁸ Until the revised version of chapter <797> is official, organizations may choose either to use the 2008 version of chapter <797> as guidance for handling of hazardous drugs or to adopt the currently informational chapter <800>.

Accreditation standards

Effective July 2020, the Joint Commission approved changes to its National Patient Safety Goals for all applicable accreditation programs.¹⁹ Revisions have also been made to Joint Commission standards related to medication titration orders; these revisions went into effect on January 1.²⁰ The organization has also released a response to frequently asked questions to provide guidance on therapeutic duplication and how it should be handled,²¹ and a Quick Safety advisory that provides information on the benefits of telehealth, as well as its barriers and challenges.²²

Controlled substances

The Drug Enforcement Administration (DEA) Diversion Control Division has issued an updated edition of the *DEA Pharmacist's Manual*.²³ The manual is a guide to help pharmacists understand the federal Controlled Substances Act (CSA) and its implementing regulations as they pertain to the pharmacy profession. The CSA Registrant Database is now available directly from the DEA at no charge.²⁴ The database, which will be updated nightly, will provide secure, efficient access to CSA data.

As a result of the growing number of states that have legalized marijuana for medicinal use, pharmacies' cannabidiol (CBD) prescription practices are facing increased scrutiny at the federal level. Pharmacies that fill CBD prescriptions based on state law should have policies and procedures specific to CBD in place.

The EPA final rule governing management standards for hazardous waste pharmaceuticals and amending the nicotine listing went into effect on August 21, 2019, six months after its publication in the *Federal Register*, in nonauthorized states (Iowa and Alaska), Indian Country, and US territories (except Guam).²⁵ In authorized states, the amendment to the nicotine listing is effective only after the state adopts the amendment.²⁶ Authorized states must adopt Subpart P by July 1, 2021. In states and territories that require legislative action for a statutory amendment, the deadline for legislative action to adopt the more stringent rules is July 1, 2022.²⁶ The prohibition on disposing of hazardous waste pharmaceuticals via a sewer system is promulgated under the authority of Hazardous

and Solid Waste Amendments, and is effective in all states 6 months after publication of the rule in the *Federal Register*, regardless of whether the state is authorized or has adopted Subpart P.

- 1 Food and Drug Administration. Wholesale distributor verification requirement for saleable returned drug product and dispenser verification requirements when investigating a suspect or illegitimate product-compliance policies; guidance for industry; availability. *Fed Regist.* 2020;85(206):67550-67552. Accessed November 11, 2020. <https://www.federalregister.gov/documents/2020/10/23/2020-23524/wholesale-distributor-verification-requirement-for-saleable-returned-drug-product-and-dispenser>
- 2 PDSA Q&A on dispenser requirements under DSCSA. Pharmaceutical distribution security alliance. October 14, 2020. Accessed November 11, 2020. <https://pdsaonline.org/resource/pdsa-qa-on-dispenser-requirements-under-dscsa>
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Advancing pharmacy practice through advocacy

Health care advocacy, particularly for pharmacy, has grown in importance as drug costs, and concerns about drug costs, have continued to grow. With the onset of COVID-19, the attention devoted to advocacy has reached unprecedented heights, reinforcing the need for pharmacists to elevate their voices in this expanding area of practice. At Vizient, we are extremely fortunate to have a **Public Policy and Government Affairs team** based in Washington, DC, that engages with legislators and regulators on any and all health care topics. During the pandemic, these established relationships with organizations such as the FDA, CMS, DEA, Federal Emergency Management Agency, and many others have enabled us to articulate critical member and patient needs such as the need for a more secure and resilient supply chain.

We know that a great deal of legislative and regulatory attention will be devoted to post-pandemic recovery of both public health and the economy. Furthermore, the new leadership in the executive branch means there will be changes in the government's approach to health care.

Numerous issues that affect pharmacy (high drug costs, drug shortages, etc) remain high on the list of health care concerns. Pharmacy leaders should be vigilant in watching for and seizing opportunities to advocate for their specific concerns.

COVID-19 recovery and more

As noted, the ongoing response to COVID-19, even with vaccine availability increasing, will continue to shape many of the legislative and regulatory efforts at the federal level. It is also reasonable to anticipate additional legislative action to deal with the economic fallout of the pandemic. In addition, regulatory bodies such as CMS and the FDA will work to advance policy agendas through annual rulemaking and to identify any temporary regulatory changes that should remain in place after the COVID-19 public health emergency ends. Further, congressional activity will also be an important factor in determining which flexibilities, including those related to care delivery such as telehealth, will remain after the emergency. In 2020, Vizient engaged in numerous advocacy efforts to support hospitals, both from a care delivery and financial sustainability perspective, and this momentum is expected to continue in 2021.

We will also maintain our substantial efforts to address the issues of drug shortages, supply chain resiliency, and the impact of foreign manufacturing. As mentioned in the **acute care** section, we continue to expand our Novaplus Enhanced Supply Program and to target **essential medications** for additional resilient sourcing activities. In late October 2020,

the FDA published its first list of essential medications, demonstrating awareness of the need to identify products of greatest concern for supply disruption.¹ Vizient has already **communicated** with the FDA about this list, the need for greater transparency in pharmaceutical manufacturing, and opportunities for ongoing collaboration.

Non-COVID-19 issues

It is also important to be aware that the policy goals of several health care-related federal legislative and regulatory actions focus on increasing competition and reducing patient spending, particularly when it comes to health care and drug costs. Complying with these efforts may result in additional workload for organizations. In response to the growing interest in price transparency, a final rule from CMS that requires all hospitals to make public their standard charges for all items and services they provide in a machine-readable format became effective on January 1.² The final rule also requires hospitals to publicize standard charges for at least 300 "shoppable services" (i.e., services than can be scheduled in advance by a health care consumer).²

340B

The 340B program remains one of the most important and talked-about programs for mitigating the high cost of pharmaceuticals and preserving access to care for underserved patient populations. Even during the pandemic, this program has received attention: Several pharmaceutical manufacturers have limited access to 340B drug prices for contract pharmacies of covered entities or required covered entities to disclose information about prescriptions filled by contract pharmacies. Much of the controversy about these actions centers on the extent to which contract pharmacies, frequently large chains, should be able to generate revenue from this program. Vizient enumerated the detrimental effects on patient care caused by these limitations in a letter to then-Secretary of Health and Human Services Alex Azar. Vizient has also recently published recommendations for members preparing responses to these actions and advises continued vigilance in this area.

Unapproved drugs

Just before the initial pandemic shutdown, leaders from the Vizient government affairs and pharmacy teams met with senior federal officials to provide insights on the negative unintended economic consequences of the FDA's Unapproved Drugs Initiative. Specifically, the UDI has led to

exponential price increases for drugs that until recently had never received formal approval as safe and effective from the FDA. This effort by the FDA to ensure that licensed pharmaceuticals meet similar regulatory standards encourages manufacturers of unapproved drugs to submit abbreviated applications. However, the current system of patents and marketing exclusivities has allowed some suppliers to protect these longstanding products from competition for up to 20 years.³

The drug that most clearly exemplifies this unintended consequence is vasopressin, a molecule that has been in use since the 1920s but only received formal licensing in 2014 — after which the WAC for the newly licensed version increased by more than 1,600%.³ Vizient member data show that during the initial COVID-19 outbreak, vasopressin was the second most commonly used drug and the fifth most commonly purchased drug for inpatient use.

On November 20, President Trump announced that the UDI program will be terminated. Vizient analysis found that ending the program will save the US health care system \$7.5 billion over a 5-year period, and \$19 billion if market exclusivity were ended for the 5 drugs approved under the UDI.

While we do not know exactly how the new administration will respond, the termination of the UDI demonstrates the incredible importance of advocacy and of our power to amplify the collective voices of Vizient members on critically important initiatives.

Payer influence on prescribing

Finally, it is important to recognize that advocacy efforts should go beyond communicating with legislative and regulatory bodies. It is an essential aspect of engagement with other health care supply chain stakeholders. One of the most important needs for such engagement is in relation to the effect insurers and other payers are exerting on providers through coverage determinations. For instance, lack of payer coverage remains the most common barrier to biosimilar adoption among Vizient members.⁴ Another example is “white bagging” (i.e., shifting drug coverage from the medical to the pharmacy benefit). Several large payers have recently resumed efforts to limit the extent to which hospitals and health systems can be reimbursed for the delivery of infusions administered by health care providers.⁵ Vizient plans to conduct a survey of our members on the issue of white bagging and will be sharing the findings both within the membership and publicly.

Neither of these issues is likely to be resolved by legislative action any time soon. Therefore, advocacy by pharmacy leaders, whether to their colleagues who manage payer agreements or even to insurers themselves, is critical.

Recommendations for strategic advocacy

Our Public Affairs and Government Relations office in Washington, DC, works to ensure that Vizient members are up to date on potential regulatory and legislative changes, issuing a biweekly Washington Update and maintaining a [Public Policy and Government Relations page](#) on the Vizient website that offers information about critical legislative and regulatory priorities. We encourage Vizient pharmacy members to devote attention and advocacy effort to several critical issues in 2021:

- **COVID-19:** Although vaccination has begun, there is still much work to be done to repair the economy. As the new government convenes, we expect that additional actions will be directed at responding to COVID-19 and better preparing the health care system for future disruptions.
- **Drug pricing:** Although a divided government will likely prevent seismic changes in drug cost management, the issue has bipartisan support, so we can expect to see additional discussions and potentially new legislative or regulatory changes or further modifications of existing policy. The same day President Trump announced the end of the UDI, he also communicated the launch of the Most Favored Nation approach to CMS reimbursement. While the influence of the new administration and anticipated legal challenges will affect the implementation of this model, additional legislative action should be anticipated.
- **Transparency:** Visibility into the location of drug manufacturing, who benefits from drug pricing programs, and how much providers charge patients for particular services will likely be a persistent theme of the new administration and Congress. Vizient members should examine all legislative and regulatory initiatives to determine what additional transparency elements are required and how the increased disclosure will affect them and their patients.

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Theranostics

One major topic of conversation in the nuclear medicine community lately is theranostics — a new approach to diagnostic nuclear medicine. Traditionally, diagnostic imaging focuses on the physiological function of the targeted organ. A radiopharmaceutical used in diagnostic nuclear medicine comprises a pharmaceutical and a radioactive component. The pharmaceutical component has a high affinity for the targeted organ, leading to rapid uptake once injected. The radioactive portion then acts as a “tag” that enables the equipment to capture an image of the physiological function of the organ. The most common example of this is a cardiac stress test, in which a technician injects a radiopharmaceutical with a high affinity for the heart that is tagged with technetium-99m (Tc-99), a radioactive component that is picked up by single photon-emission computed tomography (SPECT) imaging. The image allows the physician to see how the blood perfuses through the heart and evaluate ventricular ejection fractions to identify any damage.

Theranostics use the same basic concept as diagnostic nuclear medicine, but instead of a diagnostic pharmaceutical tagged by a radioactive component, it uses a therapeutic nuclear isotope. This enables not just diagnosis, but also treatment with targeted radiotherapy. One example currently on the market is Advanced Accelerator Application’s product Lutathera (Lutetium Lu 177 dotatate), which is used as therapy for somatostatin

receptor–positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs). It is likely that more theranostic agents will be released into the market in the near future as various isotopes are explored and tested. This is a very exciting development in nuclear medicine, offering patients a new treatment option.

As theranostics appear poised to play a major role in the future of nuclear medicine, hospitals and health systems must review their costs and budgets. Costs and price trends for diagnostic radiopharmaceuticals are well established; prices increase annually as a result of increasing raw material costs. These increases tend to average about 5% for SPECT isotopes. While this can vary, the average is a reasonably accurate mark to use for developing budgets. Planning for the cost of theranostics, however, will not be able to use this same strategy. Theranostics can be quite expensive, for a number of reasons: They are highly specialized and targeted radiotherapies that are new to the market. Some of them have no competitors; others use rare and expensive isotopes. For these reasons, costs can be quite difficult to predict, especially when new isotopes are approved in the middle of budget years. Factors such as costs, pricing trends, and reimbursement will become clearer over the next 5 to 10 years. In the meantime, these new and evolving treatment options provide exciting opportunities for both patients and physicians.



How close were we? Reviewing our drug price forecast accuracy

Given the increasing importance of drug budgets to hospitals' financial performance and our members' expectation of accuracy, we regularly review our previous forecasts to assess our accuracy.

Scope and methodology

To assess the variance in previous Drug Price Forecast purchase projections and the actual rate of drug price inflation, we compared the total average drug price inflation estimates, weighted by Vizient member purchases, against the actual price change for the projected period.

Each outlook projects price changes for the 12-month period beginning 6 months after the date of publication. The most

recent forecast that could be evaluated is the January 2019 edition, which projected price changes for July 2019 through June 2020.

Results in brief

Figure 9 depicts our accuracy for the last 8 editions. For the most recent forecast, the predicted overall price change was an increase of 4.3%, while the actual increase was 2.8%.

Because the individual product predictions are weighted by sales volume, products with high member spend have a large influence on the overall projection. Thus, a fraction of the total number of products accounted for a large percentage of the projection.

Figure 9. Comparison of published estimates and actual price change



Drug Price Forecast projections are for the 12-month period beginning 6 months after the publication date.

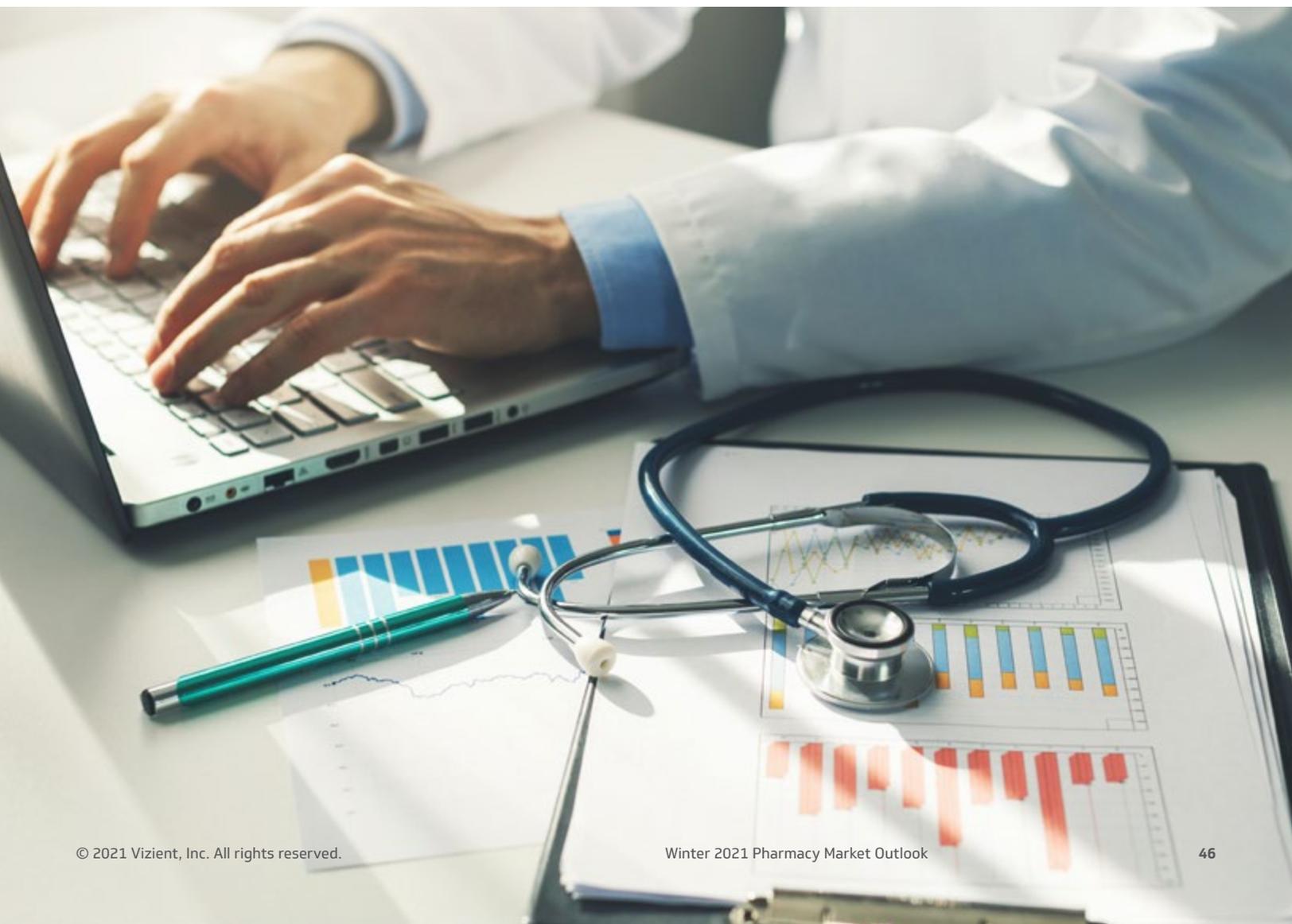
To improve our projection process, we also investigated the price projections, both understated and overstated, that contributed the most to the difference between the projected and actual price increases. The top 5, weighted by total sales, are listed in Table 18. For pegfilgrastim, dexmedetomidine, and certolizumab pegol, the lower-than-expected prices illustrate the strength of the Vizient

pharmacy portfolio: Through contract improvements, prices for these 3 products were reduced by 10.5%, 50.6%, and 10.8%, respectively.

The Vizient analytics team will continue to conduct retrospective validations of our forecasts to inform our market outlook in future and identify ways to enhance our model to increase the accuracy of our projections.

Table 18. Largest contributors to the difference between projected and actual inflation for the January 2019 Drug Price Forecast

Drug name (brand)	Projected inflation, %	Actual inflation, %	Difference, %
Pegfilgrastim (Neulasta)	0.00	-10.45	-10.45
Dexmedetomidine (Precedex)	0.00	-50.63	-50.63
Denosumab (Prolia)	9.80	4.90	-4.90
Certolizumab pegol (Cimzia)	9.00	-1.78	-10.78
Ustekinumab (Stelara)	8.00	4.90	-3.10



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