# Title Page

**Title.** National trends in prescription drug expenditures and projections for 2018

**Running Title.** Projecting future drug expenditures

## Introduction

Total healthcare spending in the United States (US) grew 4.3% in 2016 compared to 2015.[1] This was in contrast to a 2.8% increase in the US gross domestic product (GDP) over the same period. The $3.3 trillion spent on healthcare in 2016 accounted for 17.9% of the total GDP.

While the growth in healthcare expenditures in 2016 was substantial, it was lower than increases seen in 2014 and 2015 (5.1% and 5.8%, respectively), and slightly lower than predicted.[1] Spending likely slowed because of downward enrollment trends in Medicaid and private insurance, after the Affordable Care Act (ACA)-driven enrollment peak in 2015, and because of lower per enrollee costs in Medicare. Spending on retail drugs also slowed in 2016, as did spending on hospital care and physician and clinical services.

Final data on US healthcare spending in 2017 is not yet released, but healthcare spending growth is expected to rise in 2018.[2] Increased Medicare enrollment due to aging baby-boomers, and continued higher prices of medical goods and services are factors expected to contribute to this increase in growth. Prescription drugs are anticipated to play a major role in the latter, primarily as a consequence of a larger share of drug spending being accounted for by high-priced specialty drugs.[2] However, considerable debate and uncertainty remains regarding healthcare policy in the US. The Tax Cuts and Jobs Act of 2017 repealed the individual mandate of the ACA by eliminating the shared responsibility payment for failure to maintain minimum essential coverage.[3] Additionally, regulatory proposals, payment models and drug pricing schemes have been passed in some states that may impact drug pricing.[4]

The purpose of this article is to provide information to assist health-system pharmacists and other healthcare leaders involved in budgeting for drug expenses in their organizations. We examine trends in pharmaceutical expenditures, both generally and by setting, with an emphasis on nonfederal hospitals and clinics. We also consider factors that may influence future pharmaceutical spending, including new drugs and newly available generic products. Finally, drug expenditure growth for 2018 is predicted for nonfederal hospitals, clinics and overall at the national level.

## Methods

The methods used for the analysis are described in detail in the document "Methods and limitations of the annual *AJHP* paper on national trends and projections of pharmaceutical expenditures," which is provided as **supplementary material** online (available at www.ajhp.org). Data for spending in 2017 come from the IQVIA (formerly QuintilesIMS) National Sales Perspective (NSP) database, which tracks purchases of medications by hospitals, clinics, retail pharmacies, mail-service pharmacies, home health facilities, long-term-care outlets, and other health care entities. The NSP data used here were inclusive through December 31, 2017.

As in the past, for this edition of the pharmaceutical expenditures paper we conducted three focused analyses of selected drug classes thought likely to influence drug spending in hospitals or clinics. These included antimicrobials, biosimiliars, and oncology drugs.

We examined antimicrobial expenditures in 2017 compared to 2016, with a special emphasis on antibacterials and drugs indicated for the treatment of hepatitis C virus (HCV) infection. Antimicrobials were categorized based on their spectrum of activity as antibacterials, antifungals and antivirals. Antivirals were further stratified into antiretrovirals, non-human immunodeficiency virus (HIV)–targeted agents (i.e., not including those targeting HIV), and HCV antivirals.

Our analysis of biosimilars included both granulocyte colony-stimulating factor (G-CSF) products and infliximab products. We used these to assess whether a moderating effect on total expenditures had occurred with the introduction of biosimilar and competing products. The analysis of G-CSF products (i.e., filgrastim, tbo-filgrastim, filgrastim-sndz), and infliximab products (i.e., infliximab, infliximab-abda, and infliximab-dyyb) was similar to that conducted previously.[5] We examined both groups of products by quarter from January 1, 2016 to December 31, 2017 across all channels.

Finally, the third special analysis included here focused on the growth in expenditures of selected cancer drugs. We examined expenditures for immune checkpoint inhibitors (atezolizumab, avelumab, durvalumab, ipilimumab, nivolumab and pembrolizumab) within the nonfederal hospital and clinic channels in 2016 and 2017, with percentage growth relative to the previous year.

We also examined expenditures for oral cancer drugs within nonfederal hospitals and clinics. This analysis was conducted because of the frequency with which hospitals and health systems

have established specialty pharmacy services, necessitating the inclusion of expenditures for these products in drug budgets. This analysis reports the top fifteen oral oncolytic agents by expenditures in nonfederal hospitals and clinics in in 2017.

## Results

**Historical trends in prescription expenditures.** Total prescription expenditures, measured as purchases from manufacturers, across all health care settings, or sectors, in the US were $455.9 billion in 2017, a 1.7% increase compared to 2016. The distribution of drug expenditures across sectors is shown in **Table 1**. Retail pharmacy prescription spending accounted for 46.2% ($210.5 billion) of total expenditures. Mail-order pharmacies accounted for 24.1% ($110.0 billion) of total spending, followed by clinics (15.6% or $71.0 billion) and nonfederal hospitals (7.5% or $34.2 billion). The remaining sectors together accounted for less than 10% of total expenditures. As in previous years, clinics had the largest growth (10.9%) in 2017 compared to 2016. This contrasted with lower expenditures in retail pharmacies (-2.2%) and nonfederal hospitals (-0.7%) in 2017 compared to 2016.

*Factors driving growth.* There are three factors that drive growth in pharmaceutical spending – use of new products that were not available previously, price changes of existing agents, and changes in the volume of purchases (reflecting changes in utilization). In the overall market in 2017 compared to 2016, there was a drop in the volume of purchases of previously existing agents by -3.6%. This was offset by a 2.2% increase in purchases of new agents and a 3.2% increase in prices of existing agents. The net impact of these changes was a 1.7% increase in pharmaceutical expenditures in 2017.

Changes in expenditures were not the same in each sector, as shown in **Table 1**. The four sectors that accounted over 90% of spending (retail pharmacies, mail-order, clinics, and nonfederal hospitals) experienced growth due to increased prices of existing drugs. However, reductions in the volume of utilization, which occurred in all areas except clinics, counterbalanced price increases. The largest decline in utilization (-6.4%) was seen in retail pharmacies, which resulted in a net reduction in expenditures in that sector.

Clinics differed from other sectors, with growth being driven by both spending on new products (up 5.3% in 2017 compared to 2016) and more spending on existing products (up 4.6% in 2017 compared to 2016), as shown in **Table 2**. As expected, the majority of spending (78.4%) in clinics in 2017 was for injectable products.

In nonfederal hospitals the drop in total pharmaceutical expenditures in 2017 (-0.7%) was driven by reduced utilization (-5.0% in 2017 compared to 2016), which was not entirely offset by increases in spending on new products (2.8% in 2017 compared to 2016) and price increased (1.5% in 2017 compared to 2016). As in the clinic setting, injectable products accounted for a greater percentage of spending (75.2%) in nonfederal hospitals than non-injectables.

*Trends in overall drug spending.* **Figure 1** shows annual growth (increase or decrease compared to the previous year) of prescription drug expenditures in the US from 2000 to 2017 in clinics, nonfederal hospitals, and total (all sectors combined). For 2017 we observe a continued moderation in growth in the overall market (1.7%), in clinics (10.9%), and in nonfederal

hospitals (-0.7%), that was lower than anticipated.[5] Possible reasons for this are listed in the discussion section of this paper. Growth in spending on pharmaceuticals in the overall market and for nonfederal hospitals is similar to changes seen from 2007 to 2012. For nonfederal hospitals, 2017 was only the second year in the past decade (along with 2012) with negative growth.

*Top drugs overall.* In the overall market, the top 25 drugs by expenditures in 2017 are shown in **Table 3**. Adalimumab (at $17.1 billion) was the top drug, followed by insulin glargine ($9.4 billion), and etanercept ($8.8 billion). Adalimumab and etanercept (both tumor necrosis factor inhibitors) each continued a pattern of increased expenditures, growing 20.6% and 8.9%, respectively in 2017 compared to 2016 (following growth of 27.6% and 11.2% in 2016 compared to 2015). As in 2016, insulin glargine was the drug with the second highest spend in 2017, at $9.4 billion, and is one of four insulin products in the top 25. Expenditures for insulin aspart ($5.6 billion in 2017) and insulin lispro ($5.3 billion in 2017) also increased compared to 2016, 16.8% and 10.0% respectively. Spending on the combination product ledipasvir-sofosbuvir fell (-38.7%), to $6.1 billion in expenditures, while expenditures for the hepatitis C virus product emtricitabine-tenofovir disoproxil increased (18.7%) in 2017 compared to 2016. Among the top 25, other products with double-digit increases in expenditures were the combination human immunodeficiency virus (HIV) product, cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide (125.5%), apixaban (55.9%), ustekinumab (43.7%), rivaroxaban (23.5%), liraglutide (20.2%), and lisdexamfetamine (10.1%).

*Top drugs in clinics.* The top 25 drugs by expenditures in clinics followed a similar pattern in 2017 as the past, as shown in **Table 4**. Infliximab, the drug with highest spend since 2013 had $3.7 billion in expenditures in 2017, up 8.0% compared to 2016. This includes both the branded product and biosimilars. Infliximab was followed by pegfilgrastim and rituximab with spending of $3.2 billion in 2017 (up 1.8% compared to 2016) and $2.8 billion in 2017 (up 3.8% compared to 2016), respectively. Nivolumab, bevacizumab and trastuzumab rounded out the top six, each with expenditures over $2.0 billion. The drug with the largest increase in expenditures in clinics in 2017 was pembrolizumab (up 219.0% compared to 2016). That drug also grew 104.7% from 2015 to 2016. In general, biologics and cancer drugs continued to contribute the majority of the increase in drug spending in clinics in 2017. Note that additional information is provided for the top 25 cancer drugs by expenditures in clinics in 2017, as shown in **eTable 1**. Among the top 20 drugs by expenditures in clinics, those with the largest decreases in spending in 2017 were vaccines. Pneumococcal vaccine and influenza vaccine spending dropped -10.0% and -13.8% respectively.

*Top drugs in nonfederal hospitals.* The top 25 drugs based on spending in nonfederal hospitals in 2017 are shown in **Table 5**. The top 5 ranked drugs were rituximab (with $1.0 billion in expenditures), infliximab, alteplase, immune globulin and natalizumab. Infliximab spending dropped -15.6% compared to 2016, and immune globulin dropped -8.7%. As in the clinics, spending on vaccines declined. Pneumococcal vaccine dropped -11.6% and influenza vaccine dropped -20.5%. The granulocyte stimulating factor (GCSF) agents, filgrastim and pegfilgrastim also saw reductions in spending of -16.5% and -9.4% respectively. Other drugs in the top 25 with double-digit reductions in spending were daptomycin (-37.3%) and bevacizumab (-10.0%).

Large increases in spending in 2017 compared to 2016 were also observed for pembrolizumab (156.8%), vasopressin (22.0%), and iohexol (17.1%). Pembrolizumab is a drug we previously predicted would have increased spending.[5]

**Table 6** displays the top 25 therapeutic drug categories based on 2017 drug expenditures in nonfederal hospitals. Spending in these categories accounted for 94.6% of all drug spending in nonfederal hospitals in 2017. Similar to 2106, antineoplastic agents were the top category, followed by hemostatic modifiers and antiinfectives. Among the top 25 categories with the greatest increase in expenditures in 2017 compared to 2016 were drugs for neurologic disorders (30.0%), immunologic agents (16.2%), and antiarthritics (15.8%). Those with the largest decreases in spending in 2017 compared to 2016 were gastrointestinal agents (-11.2%), vascular agents (-10.9%), and antiinfectives (-9.0%).

*Trends in antimicrobials.* Almost half (48.8%) of antimicrobial expenditures were in the retail sector, followed by mail service pharmacies (25.4%), nonfederal hospitals (8.9%), clinics (8.7%) and other non-retail settings (8.2%). Antimicrobial expenditures across all sectors experienced a decrease of -8.2%, with antifungals having the largest decrease (–20.7%), followed by antibacterials (-14.8%) and antivirals (-5.9%). The portion of antibacterial expenditures attributable to each sector in 2017 was consistent with that observed in the past. However, most sectors had decreases in antibacterial expenditures in 2017 compared to 2016, with the largest reductions occurring in mail-order and retail pharmacies (–20.3% and –23.3%, respectively). Only clinics experienced growth (5.4%) in antibacterial expenditures in 2017.

Drug expenditures for HCV antivirals decreased -26.7% (compared to 2016) to $11.4 billion in 2017. The proportion of total HCV expenditures attributable to ledipasvir–sofosbuvir decreased to 53.4% in 2017 (from 63.8% in 2016). In 2017 the newer agent sofosbuvir–velpatasvir accounted for $3.1 billion in expenditures (26.8% of total HCV expenditures in 2017 compared to 7.6% in 2016), and elbasvir-grazoprevir had expenditures of $1.2 billion (10.3% total HCV expenditures in 2017 compared to 3.2% in 2016).

*Trends in biosimilars.* From 2016 to 2017, total G-CSF expenditures continued to decline from the previous year, with an -10.9% decrease in total expenditures across all channels (to a total of $730.5 million in 2017), as shown in **Figure 2A**. This decrease was likely due to shifts in utilization to competing G-CSF products, filgrastim-sndz and tbo-filgrastim, which comprised 24.9% and 18.8% of fourth quarter expenditures, respectively, and followed a pattern we have reported previously.[5]

The first US-approved monoclonal antibody biosimilar, infliximab-dyyb, was launched in the fourth quarter of 2016 and the second infliximab biosimilar, infliximab-abda, was launched in the third quarter of 2017. Since then the biosimilar infliximab products have increased market share slowly to 2.4% by the fourth quarter of 2017, as shown in **Figure 2B**. From 2016 to 2017, expenditures for all infliximab products rose by 3.2% to a total of $5.4 trillion. Unlike biosimilar G-CSF, the biosimilar infliximab products have not yet had a significant effect on total expenditures of infliximab products.

*Trends in oncology agents.* The top 20 antineoplastic agents by expenditures in clinics are listed in **eTable 1**. Expenditures for immune checkpoint inhibitors continued to be a major category of antineoplastic expenditures in clinics and in hospitals. Spending on these drugs is poised to increase even further in 2018 due to recent and ongoing FDA approvals of new agents (some based on early data and surrogate endpoints) as well as labeling changes of existing agents that expand approved indications. In 2017, expenditures in nonfederal hospitals and clinics (combined) for nivolumab rose by 17.8% compared to 2016, as shown in **eTable 2**. Pembrolizumab and atezolizumab expenditures increased by 205.3% and 207.1%, respectively, in 2017 compared to 2016. It is anticipated that expenditures of these products will increase further in 2018.

In 2017, nonfederal hospitals and clinics spent $2.92 billion on oral oncolytic agents, a 21.1% increase from the previous year. As shown in **eTable 3**, the oral oncolytic agents with the highest spend in 2017 were ibrutinib ($561.5 million, a 39.5% increase compared to 2016), followed by palbociclib ($530.0 million, a 36.8% increase compared to 2016), and abiraterone ($299.7 million, a 32.3% increase compared to 2016). Other agents with high growth in expenditures in 2017 compared to 2016 were ixazomib (57.4% increase), osimertinib (41.6% increase), and pomalidomide (26.1% increase).

**Recent and anticipated drug approvals.** Selected novel agents that may receive FDA-approval for sale in the US by the end of 2018 are shown in **Table 7**. As in past years, specialty products (including those to treat cancer) dominate this list. There are also several agents likely to be approved for migraine, a disorder that affects approximately one out of every seven adults in the

US annually.[6] Additionally, two agents will be considered for the treatment of moderate to severe pain and, because of the opioid epidemic, will likely see considerable uptake. There are agents likely to be approved in 2018 to treat multi-drug resistant bacterial infections and HIV. Further, a "universal" Factor Xa reversal agent will be considered by the FDA this year, which if approved, may increase the utilization, and expenditures for the direct oral anticoagulants apixaban, edoxaban and rivaroxaban. Together these agents could significantly increase health-system expenditures.

*Oncology drug approvals.* The FDA approved fifteen new oncolytic agents in 2017, compared to four in 2016. In **eTable 4** we list those agents approved in 2017 and the approximate cost for 28 days of therapy (or if applicable, the total cost for treatment induction), based on average wholesale price (AWP) listed in the Redbook Online.[7] It is likely that these new agents will have a considerable impact on hospital and health systems in 2018, as described further.

In 2017 three treatments were approved for acute myeloid leukemia (AML), a disease that continues to be managed predominantly by large health-systems. Two of these agents have novel mechanisms of action, and the other is a new formulation of the first-line agent. After years of only minor improvements in care of AML, these new therapies have the potential to dramatically change outcomes for patients with this severe disease. For this reason, health-systems that manage patients with AML should plan for increased drug expenditures for this disorder in 2018.

Approval of immuno-oncology agents continued to be a theme in 2017. The approval of the immune checkpoint inhibitors, avelumab and durvalumab, raised the total number of agents

within this class to five. Further, novel immuno-oncology therapies such as chimeric antigen receptor T-cell (CAR T-cell or CAR T) therapy – in which cells from patients are removed, modified in a laboratory, and re-administered to the patient to target cancer cells – have emerged as legitimate interventions to treat certain cancers.

**Generic drug trends and patent expirations**. In 2017 the FDA had another record-setting year for generics - approving 1,027 new generic drugs; 214 more than the previous record of 813 in 2016.[8] In 2017 total expenditures on generic products (including branded generics) in the US was $103.3 billion, representing 22.8% of the total drug spend. Expenditures for generics in 2017 were down -2.8% compared to 2016 and -3.9% compared to 2015.[5,9] Injectable generics accounted for 21.3% of all generic expenditures in 2017, and were -3.4% lower than in 2016. Although the noninjectable expenditures also declined in 2017 compared to 2016, the reduction of -1.8% was similar to previous years.

Glatiramer acetate is the only agent among the top 25 drugs by expenditures across all markets, **Table 3,** to have a new generic launch in 2017. Mylan Pharmaceuticals Inc. announced the FDA approval of their glatiramer acetate injection 20 mg/mL and 40 mg/mL as AP-rated, substitutable generics.[10] The approval late in 2017 has yet to have an impact on spending for glatiramer acetate, with expenditures of $4.4 billion (-0.8% compared to 2016). However, significant savings are expected in 2018.

*Generics drug trends in clinics.* In clinics there was a decrease (-3.1%) in generic spending in 2017 compared to 2016. This occurred primarily as a result of decreases in prices. Among the

top 25 drugs by expenditures in clinics, as shown in **Table 4**, sevelamer is the only agent with a new generic launch in 2017. Sevelamer spending was $0.9 billion in 2017, an increase of 5.9% compared to 2016. The launch of a first-time generic by Impax Laboratories in late October 2017 will be the largest opportunity in 2018 for reduction in spending among small molecule drugs in the clinic setting.[11]

*Generic drug trends in nonfederal hospitals.* In nonfederal hospitals generic drug spending decreased (-2.6%) in 2017 compared to 2016. This decrease occurred primarily among generic injectable drugs and was driven by reductions in price and volume of use. In 2017 there were no new first-time generic approvals for the agents in the top 25 drugs by expenditures in nonfederal hospitals, **Table 5**. Generic daptomycin, which became available in late 2016 continued to reduce expenditures for that drug in nonfederal hospitals. In 2017 daptomycin expenditures were down (-37.3%) compared to 2016. There are other oral and topical medications which received generic approval in 2017 which may impact future spending in nonfederal hospitals. These include atazanavir, atomoxetine, atovaquone, buprenorphine, eletriptan hydrobromide, ezetimibe-simvastatin, prasugrel, rasagiline, sevelamer carbonate, testosterone and tenofovir. New injectable generic agents include bortezomib and caspofungin.

*Anticipated patent expirations.* **Table 8** lists selected branded agents that are expected to lose patent protection in 2018. It is difficult to predict generic product market availability because product launch dates can be impacted by litigation, contracts for market exclusivities, and production delays. Among the branded agents with potential to lose patent expiration,

budesonide/formoterol, pregabalin, remifentanil, and tiotropium are most important in terms of ability to impact expenditures.

*Older generic drugs.* Generic medications play a vital role in reducing drug spend. However, the increasing cost of some generic products has been a concern, especially for injectables. Older generic medications with high cost growth were identified in 2017, as shown in **Table 9**. Some of the growth of expenditures for these products are due to drug shortages leading to demand-related price increases or a shift in utilization to the branded products. We have reported on this phenomenon before (i.e., with leucovorin).[12] In 2017, this was true for methylene blue (122.9% increase), ranitidine (39.6% increase), and methylprednisolone sodium succinate (14.4% increase). Additionally, product discontinuations, either due to manufacturing issues or business decisions, resulted in fewer suppliers, shortages, and/or subsequent increases in expenditures for nitroglycerin (85.5% increase), pyrimethamine (59.6% increase), sodium bicarbonate (53.8% increase), vasopressin (19.9% increase), and epinephrine (15.6% increase).

**Drug expenditure forecast for 2018.** We predict an overall (all sectors combined) increase of 3.0-5.0% in pharmaceutical expenditures in 2018 compared to 2017. We also estimate that drug spending in clinics and nonfederal hospitals will increase by 11.0-13.0% and 0.0-2.0%, respectively, in 2018 compared to 2017. These estimates for growth are consistent with other forecasts. For example, Express Scripts predicts that retail drug spending will rise 1.0-3.0% in 2018, driven mostly by growth in specialty drugs.[13] CMS has suggested that retail outlet sales of prescription drugs will rise 6.6% in 2018.[2] IQVIA predicted an overall increase of approximately 2.0-5.0% for the whole US market.[14]

## Discussion

Growth in drug expenditures in 2017 was lower than predicted.[5,14,15,17] In fact, an actual reduction in expenditures was observed in retail pharmacies and nonfederal hospitals. The decrease in drug expenditures in these settings, and overall moderation in growth, appears to have occurred primarily because of decreased utilization. Reduced use of medications may in part be due to cost-reduction strategies by providers (such as promotion of mail-order over retail pharmacy), but may also suggest that continued increases in out-of-pocket costs (copays and deductibles) are moderating utilization patterns.

Factors that are likely to increase or decrease pharmaceutical expenditures in 2018 in nonfederal hospitals and clinics are discussed below. These include the continued greater use of expensive specialty medications, growth in cancer drug spending, disease trends, the potential moderating effect of biosimilars, changes in the antimicrobial drug market, use of generics, and potential legislation on drug pricing and the 340B program.

**Specialty drugs.** Specialty drugs continue to fuel increases in overall drug spending and will do this more so in 2018. Express Scripts reported that specialty drugs accounted for 40.8% of drug expenditures for its 34 million pharmacy benefit management members in 2017.[13] Although expenditures for traditional drugs declined 4.3% in the Express Scripts report, spending for specialty drugs increased 11.3%, resulting in an overall net gain of 1.5% in 2017. Biopharmaceutical companies have invested heavily in research and development of new drugs to treat chronic, complex, or rare diseases. In 2017, the FDA approved 46 novel new drugs, the

highest number in the last ten years, and most were specialty drugs.[18] If new specialty drugs continue to outpace the rest of the market, they could account for up to 50% of total drug expenditures by 2020.

Even older specialty drugs continue to impact spending. For example, adalimumab and etanercept were major contributors to increased pharmaceutical spending in 2017. Increased expenditures for these agents may have been the result of price increases by the manufacturer in anticipation of a biosimilar entering the market, or because of increased utilization driven by significant direct-to-consumer marketing. Regardless of the cause, they are a class that requires ongoing monitoring in 2018.

The hospital outpatient clinic is the epicenter for injectable specialty medications that are billed under the medical benefit, and changes here are important to consider in 2018. Drug expenditures in outpatient clinics increased 10.9% in 2017, and specialty medications contributed heavily to this growth. This was the highest growth rate of any sector. However, there is a widespread perception among payers that hospital outpatient clinics are not competitively priced for injectable medications that are billed under the medical benefit and not subject to the competitive phenomenon (such as rebate negotiation) used to manage cost on the drug benefit side.[19] Health plans and other payers see an opportunity to reduce costs and grow their market share by redirecting infusions away from the hospital outpatient clinic to a preferred network of infusion centers or home infusion. This strategy, known as site-of-service management, was used by 48% of health plans in 2016, up from 26% in 2013. Continued spread of this strategy may reduce expenditures (and revenue) for health-systems.

A small but growing number of hospitals are establishing outpatient specialty pharmacies. Drugs such as oral oncology agents and self-injectables for inflammatory conditions contributed to the expenditure growth in the hospital clinic sector. The barriers to entry into specialty pharmacy are steep. An outpatient pharmacy presence is required, and a significant investment of time, resources, personnel, and space are needed to build a specialty pharmacy. Access to limited distribution drugs and payer networks is usually denied unless the pharmacy has one or more specialty pharmacy accreditations. Nevertheless, the hospital that has a specialty pharmacy or an infusion center has access to comprehensive patient level data in the electronic health record. The ability to report and understand patient data to improve patient outcomes is an opportunity for hospital pharmacists to participate in value-based performance contracts with payers. As more health systems establish or expand specialty pharmacies, the impact on clinic expenditures will grow.

**Cancer drugs.** With the increased number of oncology drug approvals in 2017, hospital and clinic expenditures for these agents are likely to increase in 2018. The immune-oncology agents are particularly important from an expenditure standpoint. The number of clinical indications for immuno-oncology agents (such as atezolizumab, avelumab, durvalumab, nivolumab and pembrolizumab) continues to grow, and these agents are now used for numerous tumor types. Therefore, hospitals and health-systems with cancer programs should prepare for further increases in drug expenditures in this class of medications in 2018 and beyond.

Institutions using CAR T cell therapies will also experience increases in non-drug expenditures in 2018 due to the protocols and personnel that are required to effectively monitor patients. Further, the drugs used to abate CAR T cell toxicities, such as tocilizumab, filgrastim, and intravenous immune globulin, are expensive.[20]

**Disease and Therapeutic Trends.** Forecasting drug spending for the next year should take into account medications targeted for diseases that are increasing in prevalence and other therapeutic trends. Inflammatory disorders and cancer are conditions that predominate in the specialty drug market and account for a high proportion of spending in clinics and nonfederal hospitals, as noted above. Diabetes is another condition that has contributed significantly to increased drug spending in the overall market, and will continue to do so in 2018 and beyond. As we observed, insulin products account for four of the top 25 drugs by expenditures in the overall market. These drugs are less important in terms of expenditures in the nonfederal hospital and clinic setting. Nevertheless, diabetes will continue to drive healthcare costs. Last, the increasing development and use of gene therapies is a trend that will likely have an impact on prescription drug expenditures in the future. Though perhaps not significant in 2018, this will be important for health-systems pharmacist to monitor.

**Biosimilars.** Biosimilars have shown mixed results in moderating the growth of biologic expenditures. We provided evidence of continuing reductions in total G-CSF expenditures in 2017 compared to 2016. However, the availability of two biosimilar infliximab products has not resulted in meaningful reductions in total expenditures for these products. The reasons for this is likely a combination of contracting by the reference (brand) product's manufacturer to have their

product preferred by payers and some hesitation to accept biosimilar infliximab by prescribers and patients.[21]

These challenges highlight the importance of the role of pharmacists in leading contract negotiations and patient/prescriber education to achieve cost savings on biological products. Further complicating the market is contracting between the reference and biosimilar manufacturers to delay launch of biosimilar product.[22] In a recent speech by the FDA Commissioner, the role of rebate-based contracts between benefit managers and the manufacturers of reference biologics was also identified as a barrier for biosimilar adoption. He also addressed ways that the FDA might facilitate competition among biologics, such as education programs to improve provider confidence in biosimilars.[23]

**Antimicrobials and Vaccines.** While antiinfectives remain one of the top therapeutic classes by expenditures; spending continued to decline in 2017 - just as observed in past years.[24-26] This decrease is likely attributable to increased competition among drugs to treat HCV, national initiatives to decrease antimicrobial resistance, and efforts to increase antimicrobial stewardship in the community, acute care, and long-term care settings.[25,27] It has been estimated that half of antibiotics prescribed in hospitals and one-third in primary care clinics are unnecessary.[28,29] Thus, decreased expenditures may also be partly due to the leadership of pharmacists to reduce utilization, especially among antibiotics - which have been the target of increasing stewardship efforts in both hospitals and clinics. Nevertheless, antimicrobial expenditures should continue to be monitored secondary to these changes, and also because of federal efforts to stimulate new antimicrobial drug development.

The decline in expenditures for HCV drugs will continue in 2018. Utilization and expenditures in this class tends to shift rapidly to newer agents.[30] For example, the combination agent ledipasvir–sofosbuvir, which became available in 2014, was the top drug based on expenditures in 2015 but ranked fourth in overall expenditures for 2017. This decreased market share was likely the result of competition from newer agents, the number of patients previously treated, and changes in clinical guidelines.[31] Glecaprevir-pibrentasvir and sofosbuvir-velpatasvir-voxilaprevir received FDA approval in August 2017 and July 2017, respectively, and these new agents will likely impact the HCV market in 2018.

The decline in expenditures for pneumococcal and influenza vaccines in nonfederal hospitals and clinics in 2017 is noteworthy. The changes appear to be related to reduced utilization, and may stem from loosening of Joint Commission rules requiring vaccination of hospitalized patients. Logistics around the availability of two pneumococcal vaccines, complicated administration regimens, and reimbursement concerns may have been the rationale for the change in standards. Nevertheless, reduced use of vaccines in high-risk patients does not seem like a trend favorable to public health regardless of the impact on expenditures, especially if there was not a corresponding increase in use of these vaccines in the retail setting. This should be further examined. Also on the vaccine front, a new zoster vaccine (Shingrix) was approved in late 2017 and will likely have significant expenditures in 2018.

**Generic products.** Generics provide value by reducing drug costs for the healthcare system and improving affordability for patients. Accounting for 89% of prescriptions filled in 2016, generics comprised just 26% of the cost.[8] In 2017, there was a decrease in the overall proportion of

generics as a total of the overall drug spend, and as well as the total percent growth for generics and branded generics for the injectables in the hospitals and clinics market. Reductions in the price of both injectable and noninjectable generics was observed across all market segments.

The FDA approved a record number of generics in 2017 in addition to establishing the first reauthorization of the Generic Drug User Fee Amendments (known as GDUFA II).[8] This important law authorizes the continued collection of user fees from generic drug manufacturers. Reauthorization is expected to help the FDA to continue to advance generic drugs, including complex drug products such as some inhaled or injectable products, by providing the resources to ensure access to safe high-quality and affordable generic drugs.

Generic manufacturers have struggled with the problem of drug shortages. Drug shortages have typically involved injectable products that are off-patent and have few suppliers.[32] Drug shortages are largely due to quality problems during the manufacturing process, which then halts production in order to remedy the problem. Production delays at the manufacturer and delays companies have experienced receiving raw materials and components from suppliers also contribute to shortages. In the case of a product with few competitors, this disruption in production cannot be absorbed by other companies, and demand exceeds supply, resulting in a shortage. In the case of a sole-source manufacturer, no alternatives for production exist, and clinicians must either struggle to obtain a supply of the drug, compound a drug when possible, or recommend an alternative therapy if one exists. The problem was exacerbated in 2017 because a major hurricane struck Puerto Rico in September. Many businesses which support the drug manufacturing infrastructure were damaged or destroyed. The result has been a shortage of

small-volume parenteral solution products, empty intravenous bags and other accessories needed to prepare and administer intravenous medications. The implications on drug expenditures are yet to be determined, though previous data suggest that shortages can increase costs.[33]

**340B Legislation.** One of the biggest challenges many hospitals will face in 2018 could come from legislative changes to the 340B discount drug program. Effective January 1, 2018, the Centers for Medicare and Medicaid Services (CMS) revised the Medicare hospital outpatient prospective payment system to apply an average discounted price of 22.5% of the Average Sales Price (ASP) to non-pass-through separately payable drugs purchased under the 340B Program.[34] Additional changes to the 340B program are likely. For example, on January 28, 2018, Senator Orrin Hatch (R., Utah) sent a letter to the Secretary of the Department of Health and Human Services (HHS) suggesting that the CMS, not the Health Resources and Services Administration (HRSA), have administrative oversight of all or part of the 340B program.[35] Also, a study published in the New England Journal of Medicine suggested that 340B hospitals have financial gains that are not associated with clear evidence of expanded care or lower mortality among low-income patients.[36] However, these findings were immediately disputed by 340B Health - an organization of over 1,300 hospitals and health systems that participate in the 340B drug pricing program - for lack of understanding of the 340B drug pricing program purpose and intent.[37] Regardless, it is important for pharmacy leaders to stay abreast of potential changes in the 340B program over the coming year.

**Drug prices.** Pharmaceutical prices are under continued scrutiny after egregious price increases for brand and generic drugs in recent years. Reports on industry profitability were released in

November 2017 by the Government Accountability Office and the National Academies of Science, Engineering and Medicine that demonstrated that top pharmaceutical companies have higher profitability than any other US industry.[38,39] The US Senate held three hearings on drug prices in 2017 to attempt to gain a better understanding of the issues. For now, most of the legislative activity to address prices is at the state level. At least six states (CA, FL, LA, MD, NV, and VT) have enacted drug price legislation.[39] The California law goes the farthest by requiring 60-day advance notice of price increases from manufacturers with justification of the increase and of all product launch prices. Manufacturers opposed this legislation because it does not address the large discounts given to pharmacy benefit managers and insurance companies. The Pharmaceutical Research and Manufacturers of America sued the state of California in December 2017 stating the law is unprecedented and unconstitutional.[40] Maryland prohibits a wholesaler or manufacturer to engage in price gouging for off-patent or generic drugs. Vermont requires price transparency and justification for price increases from manufacturers for up to 15 drugs selected annually by the state. Florida, Louisiana, and Nevada enacted drug price transparency laws - with Nevada's law focusing on drugs to treat diabetes. It is likely that states will continue to be the focus for drug pricing legislation since prospects for federal legislation appear to be limited at present.

**Summary.** Projecting future healthcare expenditures is difficult. Demographic, economic and political conditions, in addition to technological innovation, influence the use, price and mix of healthcare services, including medications. Health-system pharmacists and pharmacy leaders need to understand current drug spending patterns in order to budget for and manage expenditures in their own institutions. They also need to be aware of potential changes in price

due to competition (or lack thereof), emergence and adoption of new medications, as well as changing local practice patterns. Reviewing the drivers of medication use and spending, coupled with an understanding of national patterns and dynamics in the pharmaceutical supply chain, is needed to anticipate drug spend at the individual hospital or health-system level. The information provided in this report should help inform this process, but it needs to be coupled with local data and understanding.

**Limitations.** There are many limitations that should be considered when interpreting the results of the analyses conducted and of the forecast for 2018 spending described in this paper. A detailed list of limitations is provided the document "Methods and limitations of the annual *AJHP* paper on national trends and projections of pharmaceutical expenditures," which is provided as **supplementary material** online (available at www.ajhp.org).

## Conclusion

We project a 3.0-5.0% increase in total drug expenditures across all settings, a 11.0-13.0% increase in clinics, and a 0.0-2.0% increase in hospital drug spending in 2018. Health-system pharmacy leaders should carefully examine their own local drug utilization patterns to determine their own organization's anticipated spending in 2018.

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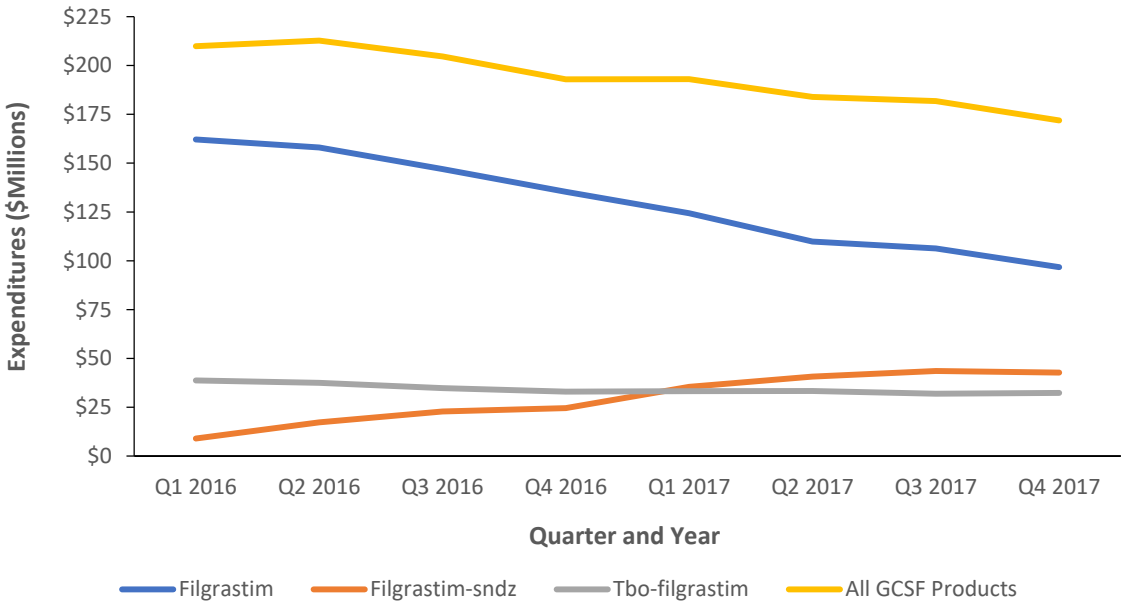
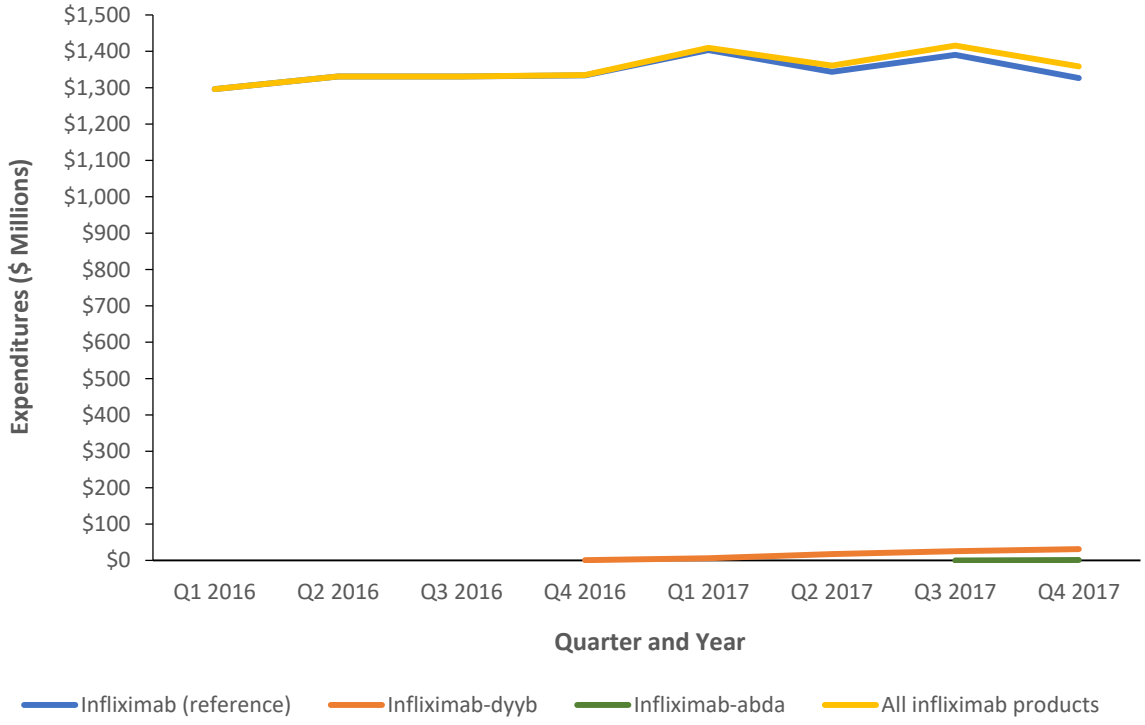
**Figure 1.** Annual growth in drug expenditures compared to previous year, 2000–2017.

**Figure 2.** Expenditures of biosimilar products from 2016 to 2017 by quarter across all channels; (A) GCSF products and (B) infliximab products

A




B



| **Table 1.** Prescription Drug Expenditures and Growth by Sector in 2017 | | | |
|---|---|---|---|
| **Sector**[a] | **2017 Expenditures ($ Millions)** | **Percent of Total Expenditures** | **Percent Change from 2016** |
| Retail pharmacies | 210,497 | 46.2 | -2.2 |
| Mail-order pharmacies | 109,971 | 24.1 | 4.5 |
| Clinics | 70,997 | 15.6 | 10.9 |
| Nonfederal hospitals | 34,197 | 7.5 | -0.7 |
| Long-term care | 16,669 | 3.7 | 0.9 |
| Staff-model HMOs | 5,634 | 1.2 | 10.2 |
| Home healthcare | 4,041 | 0.9 | 7.2 |
| Federal facilities | 2,617 | 0.6 | -8.0 |
| Other | 1,319 | 0.3 | 2.8 |
| **Total** | 455,942 | | 1.7 |

Footnotes

[a]Retail pharmacies include standalone chain and independent stores, as well as mass merchandisers and food and convenience stores with a licensed pharmacy. Mail-order pharmacies include licensed mail service pharmacies, including both private-sector and federal facilities. Clinics include physician offices and outpatient clinics, including general, family medicine, and specialty clinics covering oncology, nephrology, dialysis, family planning, orthopedics, and urgent care centers. Nonfederal hospitals include all non-federally-owned facilities licensed as hospitals, including inpatient treatment and rehabilitation facilities, in addition to general and specialty acute care institutions. Long-term care includes nursing homes

and residential care facilities. Staff-model health maintenance organizations (HMOs) include closed-panel HMO pharmacies and hospitals, union clinics and pharmacies, and workers' compensation clinics. Home healthcare includes licensed home health organizations and visiting nurse entities. Federal facilities include Public Health Service and other federal hospitals, and US ships at sea (Veteran's Health Administration facilities are normally included in the federal facility sector, but data on expenditures were not available after December 31, 2013). Other covers a variety of otherwise unclassified government accounts, as well as entities such as jails, prisons, and veterinary hospitals and clinics.

**Table 2.** Factors Driving Growth of Pharmaceutical Expenditures in Clinics and Nonfederal Hospitals in 2017, by Product Category[a]

| Product Category | Clinics | | | | Nonfederal Hospitals | | | |
|---|---|---|---|---|---|---|---|---|
| | Total Percent Growth | Percent Growth Due to Factor | | | Total Percent Growth | Percent Growth Due to Factor | | |
| | | New Products | Price | Volume and mix | | New Products | Price | Volume and mix |
| All products | 10.9 | 5.3 | 0.9 | 4.6 | -0.7 | 2.8 | 1.5 | -5.0 |
| Injectables | 11.5 | 6.2 | 1.3 | 3.9 | -1.1 | 3.3 | 1.0 | -5.4 |
| Brands | 11.8 | 6.6 | 2.0 | 3.2 | 0.9 | 3.6 | 3.1 | -5.9 |
| Generics | 3.1 | 6.5 | -7.6 | 4.2 | -5.4 | 4.0 | -6.0 | -3.5 |
| Branded generics | 15.1 | 0.6 | -0.3 | 14.8 | -6.5 | 0.7 | -1.2 | -6.0 |
| Noninjectables | 8.8 | 2.1 | -0.4 | 7.1 | 0.7 | 1.0 | 3.2 | -3.5 |
| Brands | 11.1 | 1.7 | 2.1 | 7.3 | 2.7 | 0.5 | 6.8 | -4.7 |
| Generics | -4.2 | 4.7 | -15.6 | 6.6 | 0.1 | 3.0 | -3.8 | 0.9 |
| Branded generics | 7.9 | 1.0 | 0.8 | 6.2 | 0.9 | 0.2 | 3.3 | -2.6 |

Footnotes

[a] Total growth comprised growth attributable to 3 factors: (1) new products (products that were not on the market in the previous year), primarily newly approved and marketed agents, (2) price (changes in the unit cost of drugs that were on the market in the

previous year), and (3) volume and mix (changes in volume of utilization of existing products or changes in utilization patterns [e.g., a shift from one product to another, as when prescribing moves from brand to generic products]).

| **Table 3.** Top 25 Drugs by Expenditures Overall in 2017 | | |
|---|---|---|
| **Drug**[a] | **2017 Expenditures ($ Thousands)** | **Percent Change from 2016** |
| Adalimumab | 17,106,721 | 20.6 |
| Insulin glargine | 9,362,979 | -3.7 |
| Etanercept | 8,828,006 | 8.9 |
| Ledipasvir-sofosbuvir | 6,091,534 | -38.7 |
| Insulin aspart | 5,633,123 | 16.8 |
| Infliximab | 5,544,901 | 4.5 |
| Insulin lispro | 5,340,837 | 10.0 |
| Sitagliptin | 5,055,719 | 8.4 |
| Fluticasone salmeterol | 4,910,787 | -3.7 |
| Pregabalin | 4,909,142 | 14.5 |
| Apixaban | 4,752,043 | 55.9 |
| Glatiramer | 4,370,331 | -0.8 |
| Pegfilgrastim | 4,315,216 | -0.4 |
| Rivaroxaban | 4,300,573 | 23.5 |
| Rituximab | 4,043,763 | 3.5 |
| Emtricitabine-tenofovir disoproxil | 3,987,201 | 18.7 |
| Liraglutide | 3,938,921 | 20.2 |
| Dimethyl fumarate | 3,814,417 | 0.0 |
| Ustekinumab | 3,678,817 | 43.7 |
| Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide | 3,610,546 | 125.5 |

| | | |
|---|---|---|
| Insulin detemir | 3,352,309 | -6.5 |
| Lisdexamfetamine | 3,327,777 | 10.1 |
| Albuterol | 3,319,066 | 3.0 |
| Interferon beta 1A | 3,204,554 | -5.9 |
| Tiotropium bromide | 3,152,363 | -4.2 |

Footnote

[a] For each drug listed, the expenditures shown are the total of brand and generic products (including biosimilars) and of various dosage forms unless otherwise stated.

| **Table 4.** Top 25 Drugs by Expenditures in Clinics in 2017 | | |
|---|---|---|
| **Drug**[a] | **2017 Expenditures ($ Thousands)** | **Percent Change From 2016** |
| Infliximab | 3,743,397 | 8.0 |
| Pegfilgrastim | 3,199,813 | 1.8 |
| Rituximab | 2,802,604 | 3.8 |
| Nivolumab | 2,533,504 | 21.8 |
| Bevacizumab | 2,348,893 | -3.3 |
| Trastuzumab | 2,266,471 | 7.8 |
| Erythropoietin alpha | 1,839,876 | 1.6 |
| Denosumab | 1,823,997 | 13.3 |
| Pembrolizumab | 1,787,354 | 219.0 |
| Ranibizumab | 1,457,852 | 4.1 |
| Pneumococcal vaccine[b] | 1,415,482 | -10.0 |
| Immune globulin | 1,394,138 | 21.8 |
| Sevelamer | 901,087 | 4.2 |
| Darbepoetin alfa | 882,800 | 4.0 |
| Pertuzumab | 850,288 | 13.3 |
| Pemetrexed | 840,118 | -6.2 |
| Human papillomavirus vaccine | 749,044 | -2.6 |
| Inactivated influenza virus vaccine | 741,155 | -13.8 |
| Ipilimumab | 739,362 | 13.2 |
| Abatacept | 738,308 | 12.5 |
| Natalizumab | 724,595 | 1.5 |

| | | |
|---|---|---|
| Daratumumab | 697,269 | 101.9 |
| Cinacalcet | 612,640 | 13.5 |
| Varicella virus vaccine | 610,738 | -3.7 |

Footnote

[a] For each drug listed, the expenditures shown are the total of brand and generic products (including biosimilars) and of various dosage forms unless otherwise stated.

[b] Includes both Prevnar and Pneumovax-23.

| **Table 5.** Top 25 Drugs by Expenditures in Nonfederal Hospitals in 2017 | | |
|---|---|---|
| **Drug[a]** | **2017 Expenditures ($ Thousands)** | **Percent Change from 2016** |
| Rituximab | 1,054,510 | 2.4 |
| Infliximab | 917,449 | -15.6 |
| Alteplase | 845,755 | 6.6 |
| Immune globulin | 823,152 | -8.7 |
| Natalizumab | 747,391 | 0.9 |
| Pegfilgrastim | 733,622 | -9.4 |
| Nivolumab | 515,042 | 1.5 |
| Piperacillin-tazobactam | 482,158 | 2.4 |
| Bevacizumab | 479,920 | -10.0 |
| Trastuzumab | 475,803 | -0.1 |
| Pneumococcal vaccine[b] | 473,127 | -11.6 |
| Pembrolizumab | 405,246 | 156.8 |
| Denosumab | 349,352 | 4.9 |
| Influenza virus vaccine | 335,636 | -20.5 |
| Albumin | 326,850 | 0.3 |
| Vasopressin | 326,827 | 22.0 |
| Erythropoietin alpha | 310,480 | -2.7 |
| Daptomycin | 307,981 | -37.3 |
| Regadenoson | 292,036 | -2.0 |
| Iohexol | 287,053 | 17.1 |
| Acetaminophen (i.v. only) | 241,242 | 8.0 |

| | | |
|---|---|---|
| Bupivacaine | 225,739 | 1.0 |
| Iopamidol | 223,575 | 2.6 |
| Thymoglobulin | 223,476 | 6.7 |
| Filgrastim | 220,619 | -16.5 |

Footnotes

[a] For each drug listed, the expenditures shown are the total of brand and generic products (including biosimilars) and of various dosage forms unless otherwise stated.

[b] Include both Prevnar and Pneumovax-23.

| **Table 7.** Selected Drugs and Biologicals That Have Already or May Receive FDA-Approved Labeling in 2018[a] | | | | |
|---|---|---|---|---|
| **Drug or Biological** | **Manufacturer** | **Indication** | **Route** | **PDUFA Date** (Quarter)[b] |
| Tezacaftor, ivacaftor combination | Vertex Pharmaceuticals | Cystic fibrosis | PO | Q1 |
| Ibalizumab | Theratechnologies Inc. | Multidrug resistant HIV-1 infection | IV | Q2 |
| Burosumab | Ultragenyx Pharmaceutical Inc & Kyowa Hakko Kirin International PLC | X-linked hypophosphatemia | IV | Q2 |
| Fostamatinib | Rigel Pharmaceuticals, Inc. | Chronic or persistent immune thrombocytopenia | PO | Q2 |
| Elagolix | AbbVie | Endometriosis with associated pain | PO | Q2 |
| Iobenguane I131 | Progenics Pharmaceuticals | Pheochromocytoma and paraganglioma | IV | Q2 |
| Andexanet alfa | Portola Pharmaceuticals | Acute major bleeding associated with factor Xa inhibitors | IV | Q2 |

| | | | | |
|---|---|---|---|---|
| NER1006 | Salix Pharmaceuticals, Ltd. | Overall and right-sided colon cleansing | PO | Q2 |
| Erenumab | Amgen | Prevention of migraine | SC | Q2 |
| Avatrombopag | Dova Pharmaceuticals, Inc. | Thrombocytopenia in patients with chronic liver disease | PO | Q2 |
| Meloxicam IV | Recro Pharma, Inc. | Moderate to severe post-operative pain | IV | Q2 |
| Fremanezumab | Teva Pharmaceutical Industries Ltd., | Prevention of migraine | SC | Q2 |
| Plazomicin | Achaogen, Inc. | Complicated urinary tract infections and multidrug resistant bloodstream infections | IV | Q3 |
| Cannabidiol | GW Pharmaceuticals plc | Seizures associated with Lennox-Gastaut syndrome and Dravet syndrome | PO | Q3 |
| Binimetinib & encorafenib combination | Array BioPharma | BRAF-mutation positive melanoma | PO | Q3 |

| | | | | |
|---|---|---|---|---|
| Inotersen | Ionis Pharmaceuticals, Inc. | Hereditary ATTR amyloidosis | SC | Q3 |
| Tecovirimat | SIGA Technologies, Inc | Smallpox infection | PO | Q3 |
| Patisiran | Alnylam Pharmaceuticals, Inc. | Hereditary ATTR amyloidosis | IV | Q3 |
| Volanesorsen | Akcea Therapeutics, Inc. | Familial chylomicronemia syndrome | SC | Q3 |
| Apalutamide | Janssen Biotech, Inc. | Non-metastatic castration-resistant prostate cancer | PO | Q3 |
| Ivosidenib | Agios Pharmaceuticals, Inc. | Refractory acute myeloid leukemia | PO | Q3 |
| Darunavir, cobicistat, emtricitabine, tenofovir alafenamide combination | Janssen Research & Development, LLC | Treatment of HIV-1 infection | PO | Q3 |
| Damoctocog alfa pegol (BAY94-9027) | Bayer | Treatment of hemophilia A | IV | Q3 |

| | | | | |
|---|---|---|---|---|
| Galcanezumab | Eli Lilly and Company | Prevention of migraine | SC | Q4 |
| Doravirine | Merck | Treatment of HIV-1 Infection | PO | Q4 |
| Oliceridine | Trevena, Inc. | Moderate to severe acute pain | IV | Q4 |
| Revefenacin | Theravance Biopharma, Inc. and Mylan N.V. | Treatment of chronic obstructive pulmonary disease | INH | Q4 |

Footnotes

[a] FDA = Food and Drug Administration, INH = inhalation, IV = intravenous, PDUFA = prescription drug user fee act, PO = oral, Q = quarter, SC = subcutaneous,

[b] Extrapolated based on new drug application submission date and review status (i.e., 10 months for standard review and 6 months for priority review)

| **Table 6.** Top 25 Therapeutic Drug Category by Expenditures in Nonfederal Hospitals in 2017 | | | |
|---|---|---|---|
| **Drug Category** | **2017 Expenditures ($ Thousands)** | **Percent of Total 2017 Expenditures** | **Percent Change from 2016** |
| Antineoplastic agents | 6,202,583 | 18.1 | 3.6 |
| Hemostatic modifiers | 3,028,406 | 8.9 | -2.6 |
| Antiinfectives, systemic[a] | 2,155,723 | 6.3 | -9.0 |
| Immunologic agents | 1,959,532 | 5.7 | 16.2 |
| Blood factors | 1,821,822 | 5.3 | -6.9 |
| Biologicals | 1,792,202 | 5.2 | -6.7 |
| Gastrointestinal agents | 1,626,748 | 4.8 | -11.2 |
| Hospital solutions | 1,328,660 | 3.9 | -4.5 |
| Antiviral drugs | 1,307,310 | 3.8 | 2.1 |
| Miscellaneous | 1,153,497 | 3.4 | 8.0 |
| Diagnostic aids | 1,145,879 | 3.4 | 4.8 |
| Respiratory therapy agents | 1,110,750 | 3.2 | -4.2 |
| Anesthetics | 1,105,398 | 3.2 | -2.2 |
| Hormones | 889,967 | 2.6 | 13.1 |
| Analgesics | 713,966 | 2.1 | -6.1 |
| Neurological disorder drugs | 683,257 | 2.0 | 30.0 |
| Psychotherapeutics | 679,572 | 2.0 | -7.3 |
| Musculoskeletal agents | 666,355 | 1.9 | -0.4 |
| Antiarthritics | 606,331 | 1.8 | 15.8 |
| Cardiac agents | 523,587 | 1.5 | -7.1 |

| | | | |
|---|---|---|---|
| Vascular agents | 517,775 | 1.5 | -10.9 |
| Diabetes therapies | 435,625 | 1.3 | 4.9 |
| Anti-fungal agents | 361,960 | 1.1 | -3.8 |
| Ophthalmic preparations | 358,634 | 1.0 | 0.6 |
| Enzymes | 349,232 | 1.0 | -1.2 |

Footnote

[a] Includes mostly antibacterials with some antiparasitic agents with the latter being minimal in terms of expenditures.

| **Table 8.** Selected Potential Patent Expirations for 2018. | | |
|---|---|---|
| **Drug** | **Brand Name** | **Indication** |
| Aliskerin | Tekturna HCT | Hypertension |
| Aliskerin/amlodipine | Tekamlo | Hypertension |
| Aliskerin/hydrocholorothiazide | Tekturna | Hypertension |
| Alosetron | Lotronex | Irritable bowel syndrome |
| Azelaic acid | Finacea | Acne and rosacea |
| Azelastine | Astepro | Allergies |
| Benzoyl peroxide/clindamycin | Acanya | Acne |
| Budesonide/formoterol | Symbicort | Asthma and chronic obstructive pulmonary disease |
| Cinacalcet | Sensipar | Hyperparathyroidism |
| Dabigatran | Pradaxa | Anticoagulant |
| Dalfampridine | Ampyra | Multiple sclerosis |
| Dofetilide | Tikosyn | Antiarrhythmic |
| Efavirenz/emtricitabine/tenofovir | Atripla | HIV infection |
| Eltrombopag | Promacta | Chronic immune (idiopathic) thrombocytopenia (ITP) |
| Fentanyl | Fentora | Analgesic |
| Follitropin beta | Follistim | Ovarian stimulation |
| Fosamprenavir | Lexiva | HIV infection |
| Hydroxyprogesterone | Makena | Reduce risk of preterm birth |
| Insulin glulisine | Apidra | Diabetes mellitus |

| | | |
|---|---|---|
| Lenalidomide | Revlimid | Multiple myeloma |
| Memantine/donepezil | Namzaric | Alzheimer's disease |
| Naproxen/sumatriptan | Treximet | Migraines |
| Omalizumab | Xolair | Asthma |
| Pregabalin | Lyrica | Pain, fibromyalgia, epilepsy |
| Remifentanil | Ultiva | Sedation |
| Silodosin | Rapaflo | Benign prostatic hyperplasia |
| Solifenacin | Vesicare | Overactive bladder |
| Testosterone | Fortesta | Hormone supplement |
| Tiotropium | Spiriva | Chronic obstructive pulmonary disease |
| Treprostinil | Remodulin, Tyvaso | Pulmonary arterial hypertension |
| Vardenafil | Levitra, Staxyn | Erectile dysfunction |

**Table 9.** Top 15 Older Agents with High Growth in Expenditures within the Non-Federal Hospital and Clinic Channels in 2017.

| **Drug**[a] | **2017 Expenditures ($ Thousands)** | **Percent Change From 2016** |
|---|---|---|
| Methylene blue[b] | 64,993 | 122.9 |
| Nitroglycerin IV | 25,406 | 85.5 |
| Indocyanine green | 6,820 | 74.4 |
| Lidocaine viscous | 5,916 | 60.4 |
| Potassium Chloride | 114,570 | 59.6 |
| Pyrimethamine | 16,509 | 59.6 |
| Zinc sulfate | 5,757 | 59.6 |
| Sodium bicarbonate | 42,032 | 53.8 |
| Ranitidine | 13,414 | 39.6 |
| Fluphenazine HCl | 11,881 | 37.5 |
| Tetrabenazine | 3,895 | 36.7 |
| Thiotepa | 48,960 | 23.7 |
| Vasopressin | 382,928 | 19.9 |
| Epinephrine | 206,908 | 15.6 |
| Methylprednisolone sodium succinate | 161,354 | 14.4 |

Footnotes

[a] For each drug listed the expenditures shown are the total of brand and generic products, of various dosage forms unless otherwise stated, and from include nonfederal hospitals and clinics combined.

[b] Includes both “provayblue” and “methylene blue”.

## Methods and Limitations of the Annual *AJHP* Article on National Trends and Projections of Prescription Drug Expenditures

### Methods

This paper examines both historical trends in drug expenditures and expected changes in the drug marketplace that may influence drug expenditures in nonfederal hospitals, clinics and the overall domestic marketplace for prescription pharmaceuticals, including anticipated new drug approvals and patent expirations. Data for the analysis of historical trends in expenditures are obtained from the IQVIA (formerly QuintilesIMS) National Sales Perspectives (NSP) database through December 31 of the previous calendar year.

The NSP is a statistically valid audit that projects 100% of the purchases in every major class of trade and distribution channel for prescription pharmaceuticals, nonprescription products, and select self-administered diagnostic products in the US, measuring both unit volume and invoice dollars. It is derived from annual transactions from pharmaceutical manufacturers to wholesaler distribution centers for sales to nonfederal hospitals, clinics, retail pharmacies, mail-service pharmacies, home health facilities, long-term-care outlets, and other entities. The sectors included in the report are defined as follows: 1) retail pharmacies, which include standalone chain and independent stores, as well as mass merchandisers and food and convenience stores with a licensed pharmacy; 2) mail-order pharmacies, which include licensed mail service pharmacies, including both private-sector and federal facilities; 3) clinics, which include physician offices and outpatient clinics, including general, family medicine, and specialty clinics covering oncology, nephrology, dialysis, family planning, orthopedics, and urgent care centers; 4) nonfederal hospitals, which include all nonfederally-owned facilities licensed as hospitals,

including inpatient treatment and rehabilitation facilities, in addition to general and specialty acute care institutions; 5) long-term care, which includes nursing homes and residential care facilities; 6) federal facilities, which include Public Health Service, and other federal hospitals, and US ships at sea (note: Veteran's Health Administration facilities were previously included in the federal facility sector but were not available after December 31, 2013); 7) home care, which includes licensed home health organizations and visiting nurse entities; 8) staff-model health maintenance organizations (HMO), which includes closed-panel HMO pharmacies and hospitals, union clinics and pharmacies, and workers' compensation clinics; and 9) other, which covers a variety of otherwise unclassified government accounts, as well as entities such as jails, prisons, and veterinary hospitals and clinics.

All drug dosage forms are included in the analyses conducted (except where noted) and drug class groupings by therapeutic class are based on IQVIA's proprietary Uniform System of Classification (USC).[1]

For all drug expenditures data from NSP we report total dollars spent as well as growth - the latter being the percentage change (increase or decrease) in expenditures compared to the previous 12 months. All of the analyses are based on the previous full calendar year. The historical analyses include data on expenditures across all pharmaceutical distribution channels (e.g., retail, mail-order, etc.). Within channels we categorize factors that drive changes in pharmaceutical expenditures into: (1) new products, (2) price inflation, and (3) volume and mix. The "new products" category represents growth in expenditures attributable to products that were not on the market in the comparison time period (i.e., previous year)—primarily newly approved

and marketed agents. Growth in prescription drug expenditures attributable to price inflation refers to changes in the unit cost of drugs that were previously on the market in the comparison time period (i.e., the change in price from one year to the next). The "volume and mix" category combines changes in volume of utilization of existing products (i.e., changes in the number of users, number of days of therapy, or number of doses of therapy per day) and changes in utilization patterns (i.e., from one product to another). An example of mix is when prescribing moves from brand to generic products, resulting in reduced expenditures. The factors influencing growth described above are also examined across product types – including injectables and noninjectables; and brands, generics, and branded generics.

We also examine the top 25 medications based on expenditures, and the medications with the greatest growth in expenditures compared to the previous year, in nonfederal hospitals, clinics, and overall (all channels or sectors combined). In these analyses, expenditures for each drug were totaled for all brand and generic products and the various dosage forms. Because the primary focus of this forecast is drug expenditures in hospital and clinics, we analyze trends in these sectors in more detail – including by therapeutic category.

Each year we also conduct separate analyses of selected drug classes thought likely to significantly influence drug spending in hospitals or clinics. The subject of these focused, or special analyses, vary from year to year. Such analysis have included antimicrobials, antineoplastics, biosimilars, and other important drug classes.

Drug approvals anticipated in the coming year are reviewed since these are expected to contribute to increased drug expenditures in the future. Drugs and biologics anticipated to be approved by the Food and Drug Administration (FDA) are identified by searching pharmaceutical/biotechnology business news for articles of interest to investors in the pharmaceutical/biotechnology industry. Once products are identified, their Prescription Drug User Fee Act (PDUFA) dates are determined by examining information in official press releases by the respective company sponsoring the drug or biologic. The "PDUFA date" is the date by which the FDA has committed to review and act on 90% of new drug applications (NDA) or biologics license applications (BLA). This may be a decision to approve or not approve a drug or biologic.[2,3] In the event that no explicit PDUFA date was mentioned in the official press release, the date is extrapolated by adding a 6-month (for priority reviews) or 10-month timeframe (for standard reviews) to the 60-day NDA or BLA filing date. Drugs or biologics that had negative FDA committee reviews at the time the paper is prepared are not included. Additionally, agents already FDA approved for other indications (without major differences in drug delivery) are also excluded.

In some analyses we also examine drugs approved under "breakthrough" status. In addition to containing the fifth PDUFA authorization (which spans fiscal years 2013-2017), the FDA Safety and Innovation Act (FDASIA) of 2012 promoted the expedited approval of innovative medications by allowing the FDA to designate certain potential drug candidates as "breakthrough" therapies.[4] The intent of the breakthrough designation is to expedite market approval for agents that show promise for severe or life-threatening diseases based on preliminary data (e.g., results of phase 1 studies). This differs from a fast-track designation in

that breakthrough agents are expected to demonstrate substantial improvement over current standards of care. Further, there is greater collaboration between the FDA and the drug sponsor for agents reviewed under the breakthrough pathway than for other pathway designations (including fast-track status); such interaction is essential in determining the most efficient path towards market approval.

Pharmaceuticals anticipated to lose patent protection in the next year are reviewed to estimate their impact on drug expenditures. Drugs and biologics where patent protection is expected to end are identified by searching the internet for pharmaceutical and biotechnology business news articles describing such. In addition, the list of potential patent expirations published in the previous year is examined to determine if these agents were delayed and expected to lose patent protection in the coming year. The list of potential patient expirations is primarily focused on pharmaceuticals which are substantial expenditures for the entire market or those which are particularly important to the hospital or clinic setting. Additionally, data from NSP on generic drug expenditure trends are analyzed to evaluate the impact of generic availability on the agents spend. Special emphasis is placed on generic products likely to have a significant impact on expenditures for the entire market and those which of particular importance to the hospital or clinic setting.

Finally, we predict drug expenditure growth for non-federal hospitals, clinics and overall (all settings). These estimates are generated through a combination of quantitative and qualitative analyses, considering all of the trends, new drugs, patent expirations, and other major factors that are believed to influence future drug expenditures, as discussed in the paper. Projections from

other sources are also examined and considered. These inputs are evaluated by the authors collectively, and a consensus opinion is reached as to the anticipated drug expenditure growth for non-federal hospitals, clinics and overall. Growth is defined as the percentage increase in expenditures compared to the previous year and is provided as a range.

**Limitations**

Our analysis and forecast have several important limitations. The primary source of our drug expenditure trend data is the IQVIA NSP database, and while this is a very reliable dataset, there are several issues related to it to consider. First, while this database captures greater than 90 percent of all drug expenditures, the remaining portion is extrapolated to provide estimates for the entire US population. The estimates may not represent exactly the true distribution of drug expenditures. However, less than ten percent of expenditures for prescription medications are being estimated, and we do not expect this small proportion to affect our results. Furthermore, because IQVIA has a robust process to review, verify, and update data – the data that we use in this analysis may be revised in the future. Such revisions could influence the trends we report and our projections, but were not available at the time these analyses are conducted.

Because our estimate of drug expenditures in the previous year comes from a specific data source (i.e., the NSP database), it may be different than other such estimates. For example, the Centers for Medicare and Medicaid Services (CMS) publishes an annual report of national health care expenditures, which also includes an estimate of drug spending in retail outlets in the US.[5] That estimate is typically considerably lower than what we produce. This is because the IQVIA data we use includes all sectors of the market – not just retail outlets.

Our analysis includes information on new drug approvals and patent expirations, most of which comes from FDA notices and pharmaceutical company press releases. While we do our best to identify all relevant information, some drugs may be overlooked. In particular we may miss drugs that are subjected to the FDA's breakthrough category for drug approvals, which may occur quickly and for which there is no information at the time our paper is written.

Finally, besides limitations in the data and availability of information for our analyses, empiric computation of the expected future change in expenditures is limited and primarily based on the consensus opinion of the authors. Because of the uncertainty of our predictions the forecasts are expressed in ranges. However, we have analyzed the accuracy of our past predictions, and while not without error, they have been comparable to that of annual estimates from the CMS.[6] Nevertheless, we caution readers to not blindly use our financial projects as "multipliers" to calculate future expenditures in their health systems. Instead, pharmacy managers should carefully examine their own local data and trends when developing their drug budget. Other resources should also be used where applicable, such as the ASHP strategic planning forecast which is developed annually and available at http://www.ashpfoundation.org/pharmacyforecast.

Moreover, to be effective, drug-cost-management efforts should be planned and executed as a continual process, not just as a brief annual exercise when the budget is prepared and provided to hospital administration. ASHP guidelines for drug-cost management further describe the comprehensive approach necessary to effectively manage drug costs.[7] With a well-developed and multifaceted drug-cost-management plan implemented, drug expenditures can be managed with greater confidence and effectiveness.

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| **eTable 1.** Top 20 Antineoplastic Drug Expenditures in Clinics in 2017 | | |
|---|---|---|
| **Drug** | **2017 Expenditures (Thousands)** | **Percent Change from 2016** |
| Rituximab | 2,802,604 | 3.8 |
| Nivolumab | 2,533,504 | 21.8 |
| Bevacizumab | 2,348,893 | -3.3 |
| Trastuzumab | 2,266,471 | 7.8 |
| Pembrolizumab | 1,787,354 | 219.0 |
| Pertuzumab | 850,288 | 13.3 |
| Pemetrexed | 840,118 | -6.2 |
| Ipilimumab | 739,362 | 13.2 |
| Daratumumab | 697,269 | 101.9 |
| Nab-paclitaxel | 521,575 | -0.5 |
| Ibrutinib | 510,132 | 41.2 |
| Bortezomib | 474,662 | 3.1 |
| Palbociclib | 474,487 | 36.1 |
| Carfilzomib | 454,053 | -4.6 |
| Fulvestrant | 425,622 | 14.4 |
| Cetuximab | 419,917 | -11.7 |
| Ado-trastuzumab emtansine | 284,757 | 6.6 |
| Abiraterone | 281,005 | 32.4 |
| Ramucirumab | 228,795 | 8.9 |
| Cyclophosphamide | 225,748 | -9.0 |

| **eTable 2.** Immune Checkpoint Inhibitor Expenditures in Nonfederal Hospitals and Clinics | | |
|---|---|---|
| **Agent**[a] | **2017 Expenditures (Thousands)** | **Percent Change**[b] |
| Nivolumab | 3,048,546 | 17.8 |
| Pembrolizumab | 2,192,600 | 205.3 |
| Ipilimumab | 909,491 | 12.5 |
| Atezolizumab | 451,120 | 207.1 |
| Avelumab | 20,357 | 0[c] |
| Durvalumab | 17,607 | 0[c] |
| Total | 6,639,721 | 55.8 |

Footnotes

[a] For each drug listed the expenditures shown are the total of brand and generic products and of various dosage forms unless otherwise stated.

[b] Percent increase or decrease in expenditures compared with previous year.

[c] No expenditures in previous year.

| **eTable 3.** Top 15 Oral Oncolytic Expenditures in Non-Federal Hospitals and Clinics | | |
|---|---|---|
| **Drug**[a] | **2017 Expenditures (Thousands)** | **Percent Change**[b] |
| Ibrutinib | 561,452 | 39.5 |
| Palbociclib | 529,967 | 36.8 |
| Abiraterone | 299,709 | 32.3 |
| Enzalutamide | 202,034 | 8.8 |
| Dasatinib | 128,512 | 7.4 |
| Everolimus | 96,975 | 13.0 |
| Nilotinib | 87,604 | 22.2 |
| Osimertinib | 85,892 | 41.6 |
| Imatinib | 77,263 | -30.1 |
| Erlotinib | 71,966 | -18.1 |
| Pomalidomide | 69,877 | 26.1 |
| Pazopanib | 65,972 | 17.5 |
| Ixazomib | 64,604 | 57.4 |
| Trifluridine and tipiracil | 55,023 | -3.8 |
| Sunitinib | 52,751 | -7.3 |

Footnotes

[a] For each drug listed the expenditures shown are the total of brand and generic products and of various dosage forms unless otherwise stated.

[b] Percent increase or decrease in expenditures compared with previous year.

| **eTable 4.** Oncology Agents That Received FDA-Approved Labeling in 2017[a] | | | |
|---|---|---|---|
| **Drug** | **Tumor Type** | **Route** | **Approximate price for 28 days of therapy ($)[b]** |
| Abemaciclib | Breast cancer | PO | 13,136 |
| Acalabrutinib | Mantle cell lymphoma | PO | 15,741 |
| Avelumab | Bladder, Merkel cell | IV | 12,823 |
| Axicabtagene ciloleucel | B-cell lymphomas | IV | 447,600[c] |
| Brigatinib | Lung cancer | PO | 15,960 |
| Copanlisib | Follicular lymphoma | IV | 15,120 |
| Durvalumab | Bladder cancer | IV | 11,688 |
| Enasidenib | Acute myeloid leukemia | PO | 27,856 |
| Inotuzumab ozogamicin | Acute lymphoblastic leukemia | IV | 67,320 |
| Liposome-encapsulated daunorubicin and cytarabine | Acute myeloid leukemia | IV | 27,900[c] |
| Midostaurin | Acute myeloid leukemia | PO | 19,067 |
| Neratinib | Breast cancer | PO | 12,818 |
| Niraparib | Ovarian cancer | PO | 17,841 |
| Ribociclib | Breast cancer | PO | 13,534 |
| Rituximab and hyaluronidase human | B-cell lymphomas | SC | 11,563 |
| Tisagenlecleucel-T | Acute lymphoblastic leukemia | IV | 570,000[c] |

Footnotes

[a] FDA = Food and Drug Administration, IV = intravenous, PO = oral, SC = subcutaneous

[b] Approximate cost was calculated based on average wholesale price listed in the Redbook Online.[40] For drugs that are dosed by weight or body surface area, standards of 70 kg and 1.73 $m^2$ (respectively) were used.

[c] For one course of treatment