Title Page

Title. National trends in prescription drug expenditures and projections for 2017

Running Title. Projecting future drug expenditures

Author Identification Page

Glen T. Schumock, PharmD, MBA, PhD, FCCP, is Professor and Head, Department of Pharmacy Systems, Outcomes and Policy, College of Pharmacy, University of Illinois at Chicago, Chicago, IL. Email: schumock@uic.edu (corresponding author).

Potential conflicts of interest: Dr. Schumock has consulted for or received research funding from Abbvie and Astellas, and Baxter in the past three years. Dr. Schumock is an uncompensated member to the IMS Health Services Research Network Steering Committee, from which much of the data for this paper was obtained.

Edward C. Li, PharmD, MPH, BCOP, is Associate Professor, Department of Pharmacy Practice, College of Pharmacy, University of New England, Portland, ME. Email: eli.une.edu.

Potential conflicts of interest: Dr. Li has received honoraria for advising and/or speaking for Amgen, Hospira, Merck, Pfizer, and Sandoz.

Michelle D. Wiest, PharmD, BCPS, FASHP, is Vice President, Pharmacy Services, UC Health and Clinical Associate Professor, James L. Winkle College of Pharmacy, University of Cincinnati, Cincinnati, OH. Email: Michelle.Wiest@uchealth.com.

Potential conflicts of interest: None.

Katie J. Suda, PharmD, MS, is Research Health Scientist, Department of Veterans Affairs, Center of Innovation for Complex Chronic Healthcare, Edwards Hines Jr. VA Hospital, Hines, IL; and Research Associate Professor, Department of Pharmacy Systems, Outcomes and Policy, College of Pharmacy, University of Illinois at Chicago, Chicago, IL. Email: ksuda@uic.edu.

Potential conflicts of interest: None.

JoAnn Stubbings, BS Pharm, MHCA, is Clinical Associate Professor, Department of Pharmacy Systems, Outcomes and Policy, and Assistant Director – Specialty Pharmacy Services, College of Pharmacy, University of Illinois at Chicago, Chicago, IL. Email: joanns@uic.edu.

Potential conflicts of interest: None.

Linda M. Matusiak, BA, is Senior Manager, Research Support, QuintilesIMS, Plymouth Meeting, PA. Email: LMatusiak@us.imshealth.com.

Potential conflicts of interest: None.

Robert J. Hunkler, MBA, is Director, Professional Relations, QuintilesIMS, Plymouth Meeting, PA. Email: RHunkler@us.imshealth.com.

Potential conflicts of interest: None.

Lee C. Vermeulen, BS Pharm, MS, FCCP, FFIP, is Professor of Medicine and Pharmacy, and Director, Office of Value and Innovation in Healthcare Delivery, University of Kentucky College of Medicine, Center for Health Services Research, Lexington, KY. Email: Lee.Vermeulen@uky.edu.

Potential conflicts of interest: Mr. Vermeulen is an uncompensated member to the IMS Health Services Research Network Steering Committee, from which much of the data for this paper was obtained.

Acknowledgements

The authors would like to thank all of the individuals who have served reviewers for this paper and ASHP Section of Pharmacy Practice Managers for supporting this effort. The statements, findings, conclusions, and views contained and expressed herein are those of the authors and do not necessarily represent the views of ASHP, the US government, VA, or of QuintilesIMS or any of its affiliated or subsidiary entities.

Abstract

Purpose. To provide a summary of pharmaceutical expenditures in 2016, with emphasis on hospitals and clinics; and to predict growth in drug spending in 2017.

Methods. The QuintilesIMS National Sales Perspectives database was used to examine drug purchases from manufacturers at the retail level through calendar year 2016. Anticipated new drug approvals, patent expirations, and other factors that may influence drug spending in hospitals and clinics in 2017 were obtained from various sources. Expenditure projections for 2017 for nonfederal hospitals, clinics, and overall (all sectors) were made based on a combination of quantitative analyses and expert opinion.

Results. Total prescription sales in the US for the 2016 calendar year were $448.2 billion, a 5.8% increase compared to 2015. More than half of the increase resulted from price increases of existing drugs. The top drug across all sectors was adalimumab with $13.6 billion in expenditures, followed by insulin glargine and ledipasvir-sofosbuvir. Prescription expenditures in clinics and nonfederal hospitals totaled $63.7 billion (a 11.9% increase) and $34.5 billion (a 3.3% increase), respectively, in 2016 compared to 2015. In nonfederal hospitals, growth in spending was driven primarily by price increases of existing drugs, whereas in clinics it was driven by increased volume. In both clinics and nonfederal hospitals, infliximab was the top drug based on spending. Clinic expenditures for nivolumab increased 258.1% in 2016 compared to 2015.

Conclusion. Drug expenditures in the US will continue to grow in 2017. We project overall prescription drug spending to rise by 6.0-8.0%, whereas in clinics and hospitals we anticipate an 11.0-13.0% and 3.0-5.0% increase respectively, in 2017. Health-system pharmacists should carefully consider the types of medications used and trends in their own institution when forecasting drug expenditures for budgetary purposes.

Introduction

Health care spending, and especially spending on medications, continues to occupy a significant position in national political and policy discussions. Recent data show that after several years of slower growth, health care spending in the United States (US) rose 5.3% to $3.03 trillion and 5.8% to $3.2 trillion in 2014 and 2015 respectively.[1] In 2015 this represented 17.8% of the US gross domestic product (GDP). A key driver of this growth was expansion of the number of people with health insurance under the Affordable Care Act (ACA), and the resulting increase in health care utilization – including prescription drugs. Spending on prescription drugs also grew faster in 2014 and 2015 than in several previous years. According to the Centers for Medicare and Medicaid Services (CMS) retail drug spending in the US increased 12.4% in 2014 to $298 billion, and 9.0% in 2015 to $324.6 billion. Prescription expenditures exceeded all other categories of national health care expenditures in rate of growth, and accounted for 10% for total health care spending.[1]

For health system pharmacist and pharmacy managers, understanding how drug expenditures may change in the future is important for accurate budgeting and planning. Historical trends in drug spending, such as those just described, clearly relate to future expenditures. Forecasting drug expenditure patterns also requires consideration of potential price changes, availability of less-expensive generic alternatives, changes in utilization (including the emergence of new indications for older products), and technology advancement that include the launch of new products filling therapeutic gaps. On a broader scale economic and health care policy can also impact future drug spending. While it has never been an easy process, recent political and market phenomenon have made the process of projecting expenditure patterns even more difficult.

On the political and policy front, the Trump administration and Republican-led Congress have indicated they plan to repeal and replace the ACA. Options for replacing the ACA – or even reforming portions of it – will require many months to develop and implement, during which time the planning efforts of insurers and health care systems will be even more uncertain.[2] Even if the ACA is not repealed, a number of legislative and regulatory proposals have been floated by the new administration that would have dramatic impact on health care and pharmaceutical utilization and expenditures, including the possibility of Federal negotiation of drug pricing for Medicare and changes to the regulatory standards for new drug approval. Unfortunately, these proposals lack meaningful detail, so planning for their impact is practically impossible at this time.

The legislative and regulatory uncertainty also extends to some recent legislative changes that are already in place, such as the 21st Century Cures Act.[3] Signed by President Obama on December 13, 2016, it is a broad biomedical research funding bill that was strongly supported by Republicans and Democrats alike. Key provisions included $4.8 billion over 10 years for the National Institutes of Health to fund key programs such as President Obama's Precision Medicine Initiative and Vice President Joe Biden's Cancer Moonshot. The program also included funding to streamline the FDA process for drug and device approval, which could make for faster development and approval of innovative, and likely very expensive, new drugs.
Market phenomena, particularly around drug pricing, also continue to challenge health system pharmacy leaders. The public and political drama that unfolded when Martin Shkreli, former CEO of Turing Pharmaceuticals, raised the price of pyrimethamine (Daraparim) from $13.50 to

$750 per tablet, has been repeated more recently with other products.[4] Absurdly high pricing of epinephrine auto-injectors (EpiPen, Mylan),[5] naloxone auto-injectors (Evzio, Kaléo),[6] and a newly approved steroid - deflazacort (Emflaza, Marathon Pharmaceuticals)[7], and other drugs have put the manufacturers of those products in the public spotlight and made them the subjects of Congressional inquiries. Despite mounting pressure, there does not seem to be an end in sight to the exploitive pricing policies of some drug manufacturers.

Health system leaders will almost certainly struggle with these and similar uncertainties in planning drug budgets for 2017 and beyond. Because all possible future impacts on spending are not known, the best strategy is to use of the information that is available for such planning. In this paper we analyze drug expenditures in 2016, and review factors likely to influence prescription drug spending in 2017 - including new drugs and newly available generics. Based on this information we predict drug spending for 2017 in nonfederal hospitals, clinics, and across all settings. Our intent is to provide information to aid health system pharmacists and other health care leaders in determining growth in drug expenditures in their own organizations.

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 2016 come from the 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, 2016.

For this paper we conducted three focused analyses of selected drug classes thought likely to significantly influence drug spending in hospitals or clinics - the methods for which are not described in the supplementary material. First, we examined antimicrobials expenditures in 2016, with special emphasis on antibacterials and drugs indicated for 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. HCV antiviral agents included ribavirin, interferon, telaprevir, simeprevir, sofosbuvir, boceprevir, daclatasvir, ledipasvir–sofosbuvir, elbasvir-grazoprevir, sofosbuvir-velpatasvir and ombitasvir–paritaprevir–ritonavir (available with or without dasaburvir).

Second, we analyzed expenditures for granulocyte-colony stimulating factors (GCSF) products, specifically filgrastim, tbo-filgrastim, and the biosimilar filgrastim-sndz. We assessed the impact of tbo-filgrastim and filgrastim-sndz on overall expenditures of GCSF products from January 2015 to December 2016.

Third, we assessed expenditures for immuno-oncology agents, a class of drugs that is increasingly important in treating oncologic disorders. We specifically focused on agents that stimulate the immune system by inhibiting the interaction between the Programmed Cell-Death

Protein 1 (PD-1) expressed on T-cells and its ligand, Programmed Death Ligand 1 (PD-L1), which is expressed on various tumors. For this class of agents, total expenditures across all channels were analyzed each quarter from January 2015 to December 2016. The timing of significant regulatory events (i.e., labeling updates to reflect additional indications) were identified and displayed graphically with the expenditure trends to show influence on spending.

Results

Historical trends in prescription expenditures. Total prescription expenditures in the US for the 2016 calendar year were $448.2 billion across all health care sectors, which was 5.8% higher than in 2015. **Table 1** shows the distribution of drug expenditures in 2016 across the different retail sectors. Just less than half (217.4 billion or 48.5%) of drug purchases from manufacturers were by retail pharmacies, followed by mail-order pharmacy ($103.2 billion or 23.0% of total expenditures), clinics ($63.7 billion, 14.2% of total expenditures), and nonfederal hospitals ($34.5 billion of 7.7% of total expenditures). The remaining sectors together accounted for less than 10% of total expenditures. Among the top sectors, clinics had the largest growth (11.9%) on a percentage basis in 2016 compared to 2015. Mail-order pharmacies, retail pharmacies, and nonfederal hospitals had 6.7%, 4.7% and 3.3% growth in drug expenditures, respectively, in 2016 compared to 2015.

Factors driving growth. The 5.8% growth in overall pharmaceutical expenditures in 2016 resulted mostly from increased prices of existing drugs (5.4%) and some spending on new drugs (2.2%), while utilization of existing drugs had a negative effect on spending (-1.7%). Factors that drove growth in 2016 differed by sector. In clinics the 11.9% growth in expenditures in 2016

compared to 2015 was driven mostly by increased utilization of existing products (8.1%), whereas new products and increased prices contributed 1.9% each to expenditure growth, as shown in **Table 2**. The majority of spending in clinics in 2016 was for injectable products ($49.5 billion of $63.7 billion, 77.8%), as opposed to noninjectables. Nonfederal hospitals also spent more on injectables ($25.8 billion or 74.8%) than noninjectables ($8.7 billion) in 2016. In hospitals, the 3.3% growth in expenditures in 2016 compared to 2015 was driven primarily by increased prices of existing drugs (4.6%), and to a lesser extent by new products (1.6%). Utilization of existing products (-3.0%) had a negative effect on growth of expenditures.

Trends in overall drug spending. Annual growth (increase or decrease compared to the previous year) of prescription drug expenditures in the US from 2000 to 2016 in clinics, nonfederal hospitals, and total (all sectors combined) is shown in **Figure 1**. A general decline in the rate of growth can be observed through 2012, followed by a steep increase through 2015 that moderated significantly in the past year. The growth in drug expenditures in 2016 of 5.8%, 11.9% and 3.3% for overall, clinics, and nonfederal hospitals respectively, was much lower than anticipated.[8] Possible reasons for this are listed in the discussion section of this paper.

Top drugs overall. **Table 3** shows the top 25 drugs by expenditures in 2016. Adalimumab (at $13.6 billion) was the top drug, followed by insulin glargine ($10.1 billion), and ledipasvir-sofosbuvir ($10.0 billion). Adalimumab expenditures grew 27.6% in 2016 compared to 2015, which is likely a result of price increases by the manufacture in anticipation of a biosimilar, (adalimumab-atto) entering the market.[9,10] Insulin glargine is one of 4 insulin products in the top 25, the others being insulin lispro, insulin aspart, and insulin determir. Together these products

accounted for almost $24 billion in spending in 2016. Price increases for insulin products have been a source of concern for patients and payers, and even prompted accusations of price fixing.[11,12] Among the top 25, ledipasvir-sofosbuvir was the product with the greatest reduction (-30.1%) in expenditures in 2016 compared to 2015. New and competitively priced, HCV products on the market may account for the decline in ledipasvir-sofosbuvir expenditures. The fastest growing drugs, in terms of expenditures in 2016 compared to 2015, were nivolumab (246.2% increase) and apixaban (98.0% increase).

Top drugs in clinics. The top 25 drug products based on expenditures in 2016 in clinics are listed in **Table 4**. Infliximab has been the top drug since 2013. In 2016 it had $3.5 billion in expenditures. Infliximab was followed by pegfilgrastim, rituximab, bevacizumab, trastuzumab and nivolumab – all with spending in excess of $2.0 billion. Among the top 25 clinic drugs, the biggest growth in spending in 2016 compared to 2015 was for nivolumab (258.1%) and pembrolizumab (104.7%). In general, biologics and cancer drugs contributed significantly to drug spending in clinics.

Top drugs in nonfederal hospitals. **Table 5** displays the top 25 drugs based on spending by nonfederal hospitals in 2016. The top 5 ranked drugs were infliximab (with $1.1 billion in expenditures), rituximab, immune globulin, pegfilgrastim, and alteplase. These were largely unchanged from 2015. With $511.1 million in expenditures in 2016, nivolumab experienced the largest increased spending (221.4%) compared to 2015. Vasopressin grew 109.9% compared to 2015. Those in the top 25 that experienced large decreases in expenditures in 2016 were enoxaparin (-19.3%) and filgrastim (-16.5%).

The top 25 therapeutic drug categories based on 2016 drug expenditures in nonfederal hospitals are shown in **Table 6**. These account for 94.9% of all drug spending in nonfederal hospitals. As in the past, antineoplastic agents were the top category, accounting for 17.5% of the drug spend in hospitals in 2016. Among the categories with more than $1.0 billion in expenditures the greatest increases occurred in hospitals solutions (14.3% increase compared to 2015) and immunologic agents (14.1% increase compared to 2015). The largest shrinkage was for antiinfectives (-8.1% compared to 2015).

Trends in antimicrobials. Antimicrobial expenditures across all sectors experienced a 2.3% decreased in spending in 2016 compared to 2015, with the largest decrease (-6.5%) occurring in the subcategory of antibacterials and the largest increase (4.5%) for antifungals. The portion of antibacterial expenditures attributable to each sector in 2016 was consistent with past findings, with the majority in the retail sector, followed by non-federal hospitals. With the exception of clinics (2.4% increased growth), all sectors experienced a decrease in antibacterial expenditure growth in 2016 as compared to 2015, with nonfederal hospitals and mail service pharmacies having the largest decrease at 8.1% and 9.6%, respectively.

Of particular interest among antimicrobial drugs were expenditures for HCV antivirals, which decreased 16.0%, from $18.5 billion in 2015 to $15.5 billion in 2016. Utilization (and thus expenditures) in this class tends to shift rapidly to newer agents.[13] For example, the combination agent ledipasvir–sofosbuvir, which became available in 2014, was the top drug based on expenditures in 2015 across all sectors, and accounted for the largest portion of HCV antiviral

expenditures in 2015 (77.4% of all HCV antiviral expenditures across all sectors). However, in 2016 ledipasvir-sofosbuvir experienced a 30.1% decrease in spending and accounted for a smaller proportion of HCV antiviral expenditures (64.3% of all HCV antiviral expenditures). Lower expenditures were observed for other drugs in the HCV antiviral class, with the exception of daclatasvir and the two agents approved in 2016 - elbasvir-grazoprevir and sofosbuvir-velpatasvir. Daclatasvir received FDA approval in late 2015, so expenditure growth in 2016 was primarily a function of comparing expenditures of a full year to a partial year. It is not expected to contribute significantly to expenditures in 2017 because other agents are preferred. Elbasvir-grazoprevir and sofosbuvir-velpatasvir, with 2016 expenditures of $486.1 million and $1.1 billion, respectively, appear to have taken some of the market from other HCV agents.

Trends in biosimilars. In previous reports, we analyzed expenditure trends for all available GCSF products (i.e., tbo-filgrastim and filgrastim) to assess the impact of competition on expenditures.[8,13] The first US-approved biosimilar, filgrastim-sndz, was launched in the fourth quarter of 2015. The market share of filgrastim-sndz in 2016 was 7.6%, with filgrastim declining to 74.8% as a proportion of all filgrastim expenditures. The market share of tbo-filgrastim increased slightly to 17.6% in 2016 from 15.9% in 2015. Total GCSF expenditures in all channels declined from $287.2 million in 2015 to $249.5 million in 2016. Most of this decrease is attributable to lower expenditures in the clinic and non-federal hospital sectors, as shown in **Figure 2**. During 2015 and 2016, expenditures within these channels decreased for the GCSF class, with an average net reduction in expenditures of approximately $800,000 per quarter.

Trends in immuno-oncology agents. Expenditures for immuno-oncology agents, specifically those that inhibit immune checkpoints, are projected to reach $7 billion annually by the year 2020.[14] Already in 2016, spending on this class was $4.7 billion across all sectors, which included the drugs atezolizumab, ipilimumab, nivolumab, and pembrolizumab. This represents a 159.1% increase from the $1.8 billion spent on these drugs in 2015. The major driver within this class is nivolumab, with the hxpenditure growth likely due to the fact that the product is indicated for a high-incidence tumor and received numerous labeling updates that expanded its indications over a short period of time, as shown in **eFigure 1** (available at www.ajhp.org). Pembrolizumab has a similar label to nivolumab, and while its expenditures and growth are high, they are not at the same magnitude as nivolumab. However, pembrolizumab's growth in the last quarter of 2016 far outpaced that of nivolumab (43.5% vs. 7.0%, respectively). Ipilimumab saw a growth in expenditures for the first quarter in 2016, but this has stabilized such that there was little growth throughout the rest of 2016.

Recent and anticipated drug approvals. Shown in **Table 7** are selected agents that may receive FDA-approval for sale in the US by the end of 2017. Specialty drugs and biologics dominate this list, and as in previous years, agents that treat inflammatory disorders and viral infections are numerous. Several cancer drug approvals are also anticipated in 2017, including the fourth PD-1/PD-L1 inhibitor (durvalumab), and various small-molecule drugs targeting cancers with specific mutations. A concerning omission from this list of expected approvals is any antibacterial agents. Problems with the antibiotic pipeline have been highlighted recently.[15]

While new drug approvals in 2017 will impact spending, so too may approvals that occurred in 2016. We focused on oncology drugs that were approved in 2016 because these tend to have a more significant impact on pharmacy budgets in nonfederal hospitals and clinics than other classes of drugs. Only 4 cancer drugs were approved in 2016, compared to 16 in 2015. These were atezolizumab, olaratumab, rucaparib, and venetoclax, with costs that ranged from $11,563 to $15,388 for 28 days of therapy based on average wholesale price (AWP) listed in the Redbook Online.[16] While the number of new approvals was low, this was balanced by a significant number of labeling changes to reflect new indications for already-approved drugs. For example, there were six labeling changes to immuno-oncology agents.[17] Among the four oncology drug approvals in 2016, the one most likely to impact health-system budgets is atezolizumab. Initially approved for metastatic urothelial cancer, its label was expanded to include non-small cell lung cancer patients who have progressed on platinum-based chemotherapy. Nivolumab and pembrolizumab also possess this indication in their labeling and as a result, atezolizumab will likely not make as much of a budget impact as its competitors. The other approved agents, venetoclax, olaratumab, and rucaparib are indicated for niche tumor types with a relatively low incidence. Thus, we expect that while they will increase the health-system's budget, their overall budgetary impact is not expected to be as great as compared to agents approved in previous years.

Patent expirations and generics. Generic drugs, including branded generics, accounted for 25.5% of the overall drug spend in 2016, down 1.2% compared to 2015; and comprised 16.9% and 29.7% of spending on injectables and noninjectables, respectively. In nonfederal hospitals 33.6% of the total drug spend was for generics in 2016, and the portion of spending that was on

generics was slightly higher among injectable (31.7%) compared to noninjectable (39.2%) products. The growth in generic drug spending in nonfederal hospitals from 2015 to 2016 was down compared to 2014 to 2015. Price increases drove expenditure growth among branded-generic products in nonfederal hospitals in 2016, whereas growth for non-branded generics was mostly from new products. In clinics, 15.9% of the total drug spend was for generics, and generics accounted 14.0% and 22.6% of spending on injectables and noninjectables, respectively. Increased volume of utilization is the factor that drove most of the growth in generic expenditures in clinics in 2016, although reduced prices of non-branded generics had a significant downward effect, as shown in **Table 2**.

Patent expirations in 2016 were primarily oral medications used in the outpatient setting. Generic approvals were also lower in 2016 compared to previous years. In 2016 there were 73 first generic submissions to the FDA, compared to 97 and 90 applications in 2014 and 2015, respectively.[18] Ezetimibe, imatinib mesylate, olmesartan, oseltamivir, and quetiapine fumarate extended-release all received generic approval in 2016, but none of these were in the top 25 drugs based on spending in hospitals, clinics, or overall. The biggest recent generic approval was rosuvastatin in April 2016.[19] As shown in **Table 3**, rosuvastatin dropped from the number five ranked drug to number nine based on expenditures across all sectors, a reduction of 20.9% compared to 2015.

Savings occurred in the nonfederal hospital sector in 2016 from the generic availability of daptomycin. Hospira received approval for generic daptomycin in September 2014, however, ensuing patent litigation delayed the launch. In November 2015, the US Court of Appeals for the

Federal Circuit validated the patent for Cubicin that expired on June 15, 2016, but invalidated four patents with expiration dates in 2019 and 2020.[4] Fresenius Kabi, Teva Pharmaceutical Industries Ltd. and Pfizer Injectables released daptomycin in fall 2016 resulting in a 4.9% decrease in expenditures for that drug in the nonfederal hospitals in 2016 compared to 2015, as shown in **Table 5**.

Table 8 lists selected branded agents that are expected to lose patent protection in 2017. Predicting patent expiration dates and subsequent generic drug availability is difficult because of the potential for patent litigation, agreements between brand and generic manufacturers, and manufacturing delays, among other reasons. Nevertheless, anticipating generic availability is important for projecting drug expenditures. Among those listed in **Table 8**, atazanavir, caspofungin, ertapenem, ezetimibe-simvastatin, and octreotide acetate for injectable suspension, are products that could make a difference in spending in nonfederal hospitals and clinics.

In addition to new generics that may become available, changing prices of existing generic products can impact expenditures. The rapid increase of the price of previously inexpensive generic products has been a major issue and was highlighted in a recent report by the American Hospital Association (AHA).[20] We evaluated older medications in nonfederal hospitals and clinics (combined) with high growth in expenditures in 2016 compared to 2015, as shown in **Table 9**. Pyrimethamine had the greatest overall increase in expenditures from 2015 to 2016, at 552.7%, followed by thiotepa (394.3%) and zinc sulfate (327.0%). Other items of note on this list are vasopressin and calcitonin. Vasopressin had $319.1 million in expenditures in nonfederal

hospitals and clinics combined in 2016, up 102.9% compared to 2015. Calcitonin had $114.9 million in expenditures in 2016, up 58.6% from 2015.

Drug expenditure forecast for 2016. We predict an overall (all sectors combined) increase of 6.0-8.0% in pharmaceutical expenditures in 2017 compared to 2016. We also estimate that drug spending in clinics and nonfederal hospitals will increase by 11.0-13.0% and 3.0-5.0%, respectively, in 2017 compared to 2016.

These estimates for growth are consistent with other forecasts. For example, Express Scripts predicts that retail drug spending will rise 10.3% in 2017, driven mostly by growth in specialty drugs.[21] CMS has suggested that retail outlet sales of prescription drugs will rise 5.7% in 2017.[22] QuintilesIMS has predicted an overall increase of approximately 6.0% for the whole US market.[23]

Discussion

In this paper we have analyzed specific drugs and drug classes that contributed to growth in prescription expenditures in 2016 and/or that may be expected to do so in 2017. Growth in drug expenditures in 2016 in clinics, nonfederal hospitals, and overall moderated considerably compared to 2015. Actual growth was lower than most had anticipated - including CMS, Express Scripts, and our own forecast.[8,24,25] This may in part be due to an unanticipated moderation in growth of expenditures for specialty drugs - and specifically for hepatitis C antivirals; because of fewer than expected new drug approvals; or because of cost-reduction strategies by providers, such as expanded use of biosimilars. Evidence also suggests that criticism by policymakers and

the media may have forced manufacturers to hold price increases below that which was expected given past history.[26] The lower than forecasted growth also demonstrates the difficulty of accurately predicting future drug spending in the economically and politically volatile environment of health care.[27]

Despite some moderation in the rate of growth of specialty drugs in 2015, we still anticipate these to be major contributors to future spending. In 2016 the FDA approved 22 novel agents - most of which were considered specialty drugs.[28] Among these were notable advances in the treatment of chronic HCV, plaque psoriasis, chronic lymphocytic leukemia, sarcoma, and multiple sclerosis, to name a few. Eight of the drugs were approved as "first-in-class", which is an indication of the innovative nature of the drug, and nine were approved to treat orphan diseases that affect 200,000 or fewer Americans.

While specialty drugs represent an increasing portion of new drug approvals, they are also contributing disproportionally to drug spending. Express Scripts has reported that specialty drugs accounted for three of the top five therapeutic categories in per member per year expenditures in 2016 (inflammatory conditions, oncology, multiple sclerosis).[21] QuintilesIMS has shown that overall spending on specialty medications in the US doubled from 2010 through 2015, and contributed 70 percent to overall pharmaceutical spending growth.[29] The Office of Inspector General of the Department of Health and Human Services recently reported that high cost (mostly specialty drugs and defined as costing >$1,000 per month) accounted for $33 billion (nearly two-thirds) of the total drug spend in Medicare Part D catastrophic coverage in 2015, which was three times higher than the amount spent in 2010.[30]

Despite the significant contribution of specialty drugs to overall expenditures, there are market factors (such as the withdrawal of the 340B Program Omnibus Guidelines) and barriers that may mitigate growth in hospital and clinics in the future. Specialty drug access restrictions by manufacturers and payers reduces the number and types of drugs that hospitals and clinics can dispense or administer to their patients – and thus reducing expenditures in hospitals and clinics. Of the 44 new drugs approved by the FDA in 2015, 28 (63.6%) had some form of restriction on distribution placed by the manufacturers.[31]

Payer restrictions on specialty drug access varies widely by payer and region, but one strategy that could reduce clinic expenditures is based on site of service. Site of service restrictions typically involve the payer carving-out certain infusions from the medical benefit and then promoting an alternate site of service such as home infusion, or by redirecting the site of service at the point of prior authorization. Chronic infused therapies such as infliximab and intravenous immunoglobulin were the initial focus of this effort, but now payers are also targeting more complex therapies - such as cancer drugs.[32] Examples of these strategies include payers requiring, incentivizing, or recommending patients to use alternative infusion sites, or requiring "white bagging" - where the medication is delivered from a specialty pharmacy to the infusion site. EMD Serono has reported that 44% of commercial health plans used at least one site of service strategy in 2015, up from 31% in 2014.[33] While the growing use of site of service restrictions may exert downward pressure on clinic expenditures for injectable drugs in 2017 and beyond, the resulting fragmentation of care may lead to more emergency room visits or hospital admissions for patients who need urgent infusions.

Biosimilars are also starting to reduce specialty drug expenditure growth while at the same time expanding access to important therapies.[34] For example, we found that GCSF expenditures fell by $38 million after one year due to the availability of a biosimilar. We expect this trend to continue, especially with anticipated future competition. Although savings with GCSF products bode well for the health care system, potential expenditure reductions are much greater other biosimilar products, such as adalimumab, etanercept and infliximab. At of the time of this analysis, these biosimilar products had either not yet launched or were early in the launch process and therefore had not yet impacted expenditures. The US health care system is poised for significant savings if the same discount experienced for GCSF products was applied to these three biologics, and our future reports will monitor these trends.

Other biosimilars for use in oncologic indications are also promising. Pegfilgrastim, rituximab, bevacizumab and trastuzumab are consistently listed on the list of top 25 expenditure drugs annually. Biosimilars for these agents are under development and approvals for bevacizumab and trastuzumab may occur in 2017.[35-37] However, experience with previous biosimilars would suggest that significant launch delays are likely to occur because of legal patent challenges.

Many specialty drugs are used for cancer care. A reduced number of oncology drug approvals in 2016, and the fact those new agents were for low-frequency indications, likely also contributed to the slower drug expenditure growth as compared to previous years. Though lower than 2015, growth in clinic drug expenditures in 2016 (11.9%) was partially fueled by the use of immuno-oncology agents such as nivolumab and pembrolizumab, which both agents were granted

expanded indications over the past year. In 2017, we expect an increased in the number of new oncology drugs approved by the FDA, with some for higher-incidence cancers such as lung and breast cancer. Specifically, agents such as neratinib and ribociclib are positioned to have a drastic impact on spending. However, because these agents are orally administered, expenditures will impact all sectors including mail order pharmacies and clinic-based pharmacies.

Immuno-oncology agents will continue to significantly impact expenditures in hospitals and clinics. The novel class of PD-1/PD-L1 inhibitors have had a multitude of labeling changes post-FDA approval and as indications expand for these agents, it is expected that total expenditures will continue to increase. Durvalumab's expected approval in 2017 will further increase spending in this class of medications.[38] Nivolumab is currently the expenditure leader in this class due to its more expansive label at the time of launch compared to pembrolizumab. Interestingly, pembrolizumab experienced greater growth in the last quarter of 2016 than in previous quarters. That timing coincided with the release of favorable clinical trial results and a subsequent change in the guidelines that positioned pembrolizumab as a first-line option (over nivolumab) in previously untreated non-small cell lung cancer.[39] These events will likely cause pembrolizumab's expenditure growth to be higher than that of nivolumab for 2017.

In our 2014 forecast, we reported that antimicrobial expenditures decreased over the previous 10 years.[40] Since then the anti-infective space has been dynamic - influenced by approvals for costly medications to treat HCV, national initiatives to decrease bacterial resistance, and efforts to increase stewardship programs in acute care and long-term care settings.[41] While anti-infectives remain one of the top therapeutic classes by expenditures, spending continued to diminish in

2016. This may be due in part to efforts to reduce utilization, especially among antibiotics, which have been the target of increasing stewardship efforts in both hospitals and clinics. It has been estimated that half of antibiotics prescribed in hospital settings and one-third in primary care clinics are unnecessary.[42,43]

We previously reported that HCV antivirals experienced 60.8% growth in 2015 compared to 2014. In addition, ledipasvir-sofosbuvir was the top drug overall based on expenditures in 2015, with sofosbuvir (single-agent) also in the top 25.[8] However, in 2016 the HCV antivirals had reduced expenditures for the first time since 2013.[41] Some had predicted that the number of patients treated, and thus expenditures, would begin to decline in 2017 and beyond.[44] The early decline in expenditures may be related more to price reductions as a result of competition created by multiple new HCV drugs on the market. In fact, at least on report has confirmed both a reduction in unit cost and in utilization for HCV drugs.[21] Regardless, it appears that the class may see continued reductions in expenditures in 2017.

Historically, we have seen moderation in drug expenditure growth caused by the increased availability and utilization of generic medications. However, in the past few years unexpected price increases of some older generic drugs have disrupted the norm. Such price increases have caused significant hardship for patients, providers, and payers, and have even attracted attention of legislators and policy makers. The Government Accountability Office reported recently that while on average the prices of generic drugs covered under the Medicare Part D program dropped from 2010 to 2015, there was a group of 315 drugs that experienced extraordinary price increases during that period.[45] Price increases in this group were at least 100% and, in some

cases, 1000% or more. A specific example was that of EpiPen by Mylan. The price hike from $100 to over $600 for a package of two EpiPens was the focus of public outcry in 2016, resulting in a federal investigation and a $465 million settlement paid by Mylan on allegations that it overbilled Medicaid.[5,46] Doxycycline and glyburide are two other examples. In December 2016 the US Department of Justice charged two former executives of different generic pharmaceutical companies of conspiring to fix prices and rig bids for doxycycline and glyburide.[47] This action was followed by a twenty-state federal criminal charge against six generic drug-makers, alleging that they entered into illegal conspiracies in order to unreasonably restrain trade, artificially inflate and manipulate prices and reduce competition for the two drugs.[48]

Focused attention in the hospital arena has also highlighted concerns of predatory pricing of generic medications. The AHA reported the results of a survey of all US community hospitals that found that inpatient drug costs increased 38% per admission in just three years, and that growth in unit price was primarily responsible for this increase.[20] Price increases appeared to be random, inconsistent and unpredictable - with hikes occurring for both high- and low-volume drugs - but most were generic or non-innovator drugs. Others have reported on the impact of generic drug price hikes in the hospital setting.[49] Despite these and other examples of generic drug price hikes, generics still contribute to savings in general. In their 2016 Annual Report, the Association for Accessible Medicines (formerly the Generic Pharmaceutical Association), reported that generic drugs are increasing in the contribution to the drug spend and declining in price overall, and contributed to $227 billion in savings in 2015.[50]

As we have illustrated in this paper, overall spending on drugs in the US is impacted by many different factors - the most important of which are changes in the economy, population, and the health care system. Today's tumultuous political climate makes the economy and health policy difficult to predict. While health care financing and policy in the US is uncertain at present, the US will continue to experience the long-term trend of the aging of its population and the associated increase in health care needs and spending. In the pharmaceutical market, the entry of new products (brand or generic), changes in prices of existing agents, and changes in utilization or patterns of use will also impact drug spending. As we have suggested previously, pharmacy leaders must keep abreast of important developments in health policy, health finance, technology and practice in order to be optimally prepared for changes that may influence practice and thus impact medication spending. The analyses and projections presented here focus on factors likely to influence health care spending and prescription drug expenditures in 2017, but pharmacy leaders should also carefully monitor other developments that are likely to impact their department budgets in the coming years. Additional guidance on emerging issues that may impact drug spending can be found in the ASHP Foundation Forecast 2017.[51]

Limitations. There are many limitations that should be considered when interpreting the results of the analyses conducted and of the forecast for 2017 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 6.0-8.0% increase in total drug expenditures across all settings, a 11.0-13.0% increase in clinics, and a 3.0-5.0% increase in hospital drug spending in 2017. Health-system pharmacy leaders should carefully examine their own local drug utilization patterns to determine their own organization's anticipated spending in 2017.

References

1. Martin AB, Hartman M, Washington B, Catlin A, Team NHEA. National Health Spending: Faster Growth In 2015 As Coverage Expands And Utilization Increases. Health Aff (Millwood) 2017;36:166-76.
2. Ku L, Steinmetz E, Brantley E, B B. The economic and employment consequences of repealing federal health reform: A 50 state analysis. Washington, DC: Milken Institute School of Public Health; 2017.
3. Obama signs 21st Century Cures Act. Nat Biotechnol 2017;35:6.
4. Tallapragada NP. Off-patent drugs at brand-name prices: a puzzle for policymakers. J Law Biosci 2016;3:238-47.
5. Lyon J. Significant Increases in EpiPen Price. Jama 2016;316:1439.
6. Gupta R, Shah ND, Ross JS. The Rising Price of Naloxone - Risks to Efforts to Stem Overdose Deaths. N Engl J Med 2016;375:2213-5.
7. Johnson C. An old drug gets a new price to fight a rare disease: $89,000 a year. Washington Post 2017 February 10, 2017.
8. Schumock GT, Li EC, Suda KJ, et al. National trends in prescription drug expenditures and projections for 2016. Am J Health Syst Pharm 2016;73:1058-75.
9. Humer C. Makers took big price increases on widely used U.S. drugs. Reuters 2016 April 5, 2016.
10. FDA. FDA approves Amjevita, a biosimilar to Humira. Silver Springs, MD: Food and Drug Administration; 2016.
11. Kesselheim AS, Avorn J, Sarpatwari A. The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform. JAMA 2016;316:858-71.
12. Thomas K. Drug makers accused of fixing prices on insulin. New York Times 2017 January 30, 2017.
13. Schumock GT, Li EC, Suda KJ, et al. National trends in prescription drug expenditures and projections for 2015. Am J Health Syst Pharm 2015;72:717-36.
14. Webster RM. The immune checkpoint inhibitors: where are we now? Nat Rev Drug Discov 2014;13:883-4.
15. Luepke KH, Suda KJ, Boucher H, et al. Past, Present, and Future of Antibacterial Economics: Increasing Bacterial Resistance, Limited Antibiotic Pipeline, and Societal Implications. Pharmacotherapy 2017;37:71-84.
16. RED BOOK Online [database online]. Truven Health Analytics Micromedex Solutions; 2016.
17. Approved Drugs - Hematology/Oncology (Cancer) Approvals & Safety Notifications. Center for Drug Evaluation and Research, 2017. (Accessed 2/16/2017, at http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm.)
18. ANDA generic drug approvals in 2016. 2017. (Accessed February 11, 2017, at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/ANDAGenericDrugApprovals/ucm539767.htm.)
19. FDA approves first generic Crestor. 2016. (Accessed February 11, 2017, 2017, at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm498373.htm.)
20. AHA. Trends in hospital inpatient drug costs: Issues and challenges: American Hospital Association; 2016.
21. ExpressScripts. 2016 Drug Trend Report2017 March 2015.
22. Keehan SP, Stone DA, Poisal JA, et al. National Health Expenditure Projections, 2016–25: Price Increases, Aging Push Sector To 20 Percent Of Economy. Health Affairs 2017.
23. Aitken M, Kleinrock M, Nass D. Outlook for global medicines through 2012. Parsippany, NY2016 December 2016.
24. TheExpressScriptsLab. Express Scripts 2015 Drug Trend Report2016 March 2016.

25. Keehan SP, Poisal JA, Cuckler GA, et al. National Health Expenditure Projections, 2015-25: Economy, Prices, And Aging Expected To Shape Spending And Enrollment. Health Aff (Millwood) 2016;35:1522-31.
26. Rockoff J, Loftus P. Facing criticism, drug makers keep lid on price increases. Wall Street Journal 2017 February 26, 2017.
27. Hartke PL, Vermeulen LC, Hoffman JM, et al. Accuracy of annual prescription drug expenditure forecasts in AJHP. Am J Health Syst Pharm 2015;72:1642-8.
28. Novel new drugs: 2016 summary. 2017. (Accessed February 12, 2017, 2017, at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm483775.htm.)
29. Medicine use and spending in the US. IMS Institute for Healthcare Informatices, 2016. (Accessed February 20, 2017, 2017, at http://www.imshealth.com/en/thought-leadership/quintilesims-institute/reports/medicines-use-and-spending-in-the-us-a-review-of-2015-and-outlook-to-2020.)
30. Levinson D. High-price drugs are increasing federal payments for Medicare Part D catastrophic coverage. In: General HaHSOotI, ed.January 2017.
31. Hatwig C, Thompson R, Stubbings J, G B. 340B update and challenges with limited distribution drugs. ASHP Pharmacy Practice & Policy Meeting. Baltimore, MD2016.
32. EMDSerono. EMD Serono Oncology Digest 2016. 2016.
33. EMD Serono Specialty Digest. 2016. (Accessed February 12, 2017, 2017, at http://www.specialtydigest.emdserono.com/Digest.aspx.)
34. Zelenetz AD, Ahmed I, Braud EL, et al. NCCN Biosimilars White Paper: regulatory, scientific, and patient safety perspectives. J Natl Compr Canc Netw 2011;9 Suppl 4:S1-22.
35. Jacobs I, Ewesuedo R, Lula S, Zacharchuk C. Biosimilars for the Treatment of Cancer: A Systematic Review of Published Evidence. BioDrugs 2017;31:1-36.
36. Mylan and Biocon Announce U.S. FDA Submission for Proposed Biosimilar Trastuzumab. @PRNewswire, 2017. (Accessed 2/16/2017, at http://www.prnewswire.com/news-releases/mylan-and-biocon-announce-us-fda-submission-for-proposed-biosimilar-trastuzumab-300358627.html.)
37. Amgen. Amgen and Allergan submit biosimilar biologics license application for ABP 215 to US Food and Drug Administration.: Amgen; 2016.
38. US FDA accepts first biologics license application for AstraZenecaâ™s durvalumab in bladder cancer. 2017. (Accessed 2/15/2017, at https://www.astrazeneca.com/media-centre/press-releases/2016/US-FDA-accepts-first-biologics-license-application-for-AstraZenecas-durvalumab-in-bladder-cancer-09122016.html.)
39. Reck M, Rodriguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. N Engl J Med 2016;375:1823-33.
40. Schumock GT, Li EC, Suda KJ, et al. National trends in prescription drug expenditures and projections for 2014. Am J Health Syst Pharm 2014;71:482-99.
41. Suda KJ, Halbur DJ, Hunkler RJ, Matusiak LM, Schumock GT. Spending on Hepatitis C Antivirals in the United States, 2009-2015. Pharmacotherapy 2017;37:65-70.
42. Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. Jama 2016;315:1864-73.
43. Core elements of hospital antibiotic stewardship programs. 2016. at https://www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf.)
44. PwC. Medical cost trend: Behind the numbers 2017.2016 June 2016.
45. GAO. Generic drugs under Medicare: Part D generic drug prices declined overall, but some had extraordinary price increases. In: Office GA, ed.2016.
46. Mylan. Mylan agrees to settlement on Medicaid rebate classification for EpiPen auto-injector. 2016.

47. DOJ. Former top generic pharmaceutical executives charged with price-fixing, bid-rigging and customer allocation conspiracies.: US Department of Justice; 2016.
48. Thomas K. 20 states accuse generic drug companies of price fixing The New York TImes 2016 December 15, 2016.
49. Schumock GT, Vermeulen LC. The Rising Cost of Prescription Drugs: Causes and Solutions. Pharmacotherapy 2017;37:9-11.
50. AAM. 2016 Annual Report: Association for Accessible Medicines; 2017.
51. Allen SJ, Zellmer WA, Knoer SJ, et al. ASHP Foundation Pharmacy Forecast 2017: Strategic Planning Advice for Pharmacy Departments in Hospitals and Health Systems. Am J Health Syst Pharm 2017;74:27-53.

Figure 1. Annual growth in drug expenditures compared to previous year, 2000–2016.

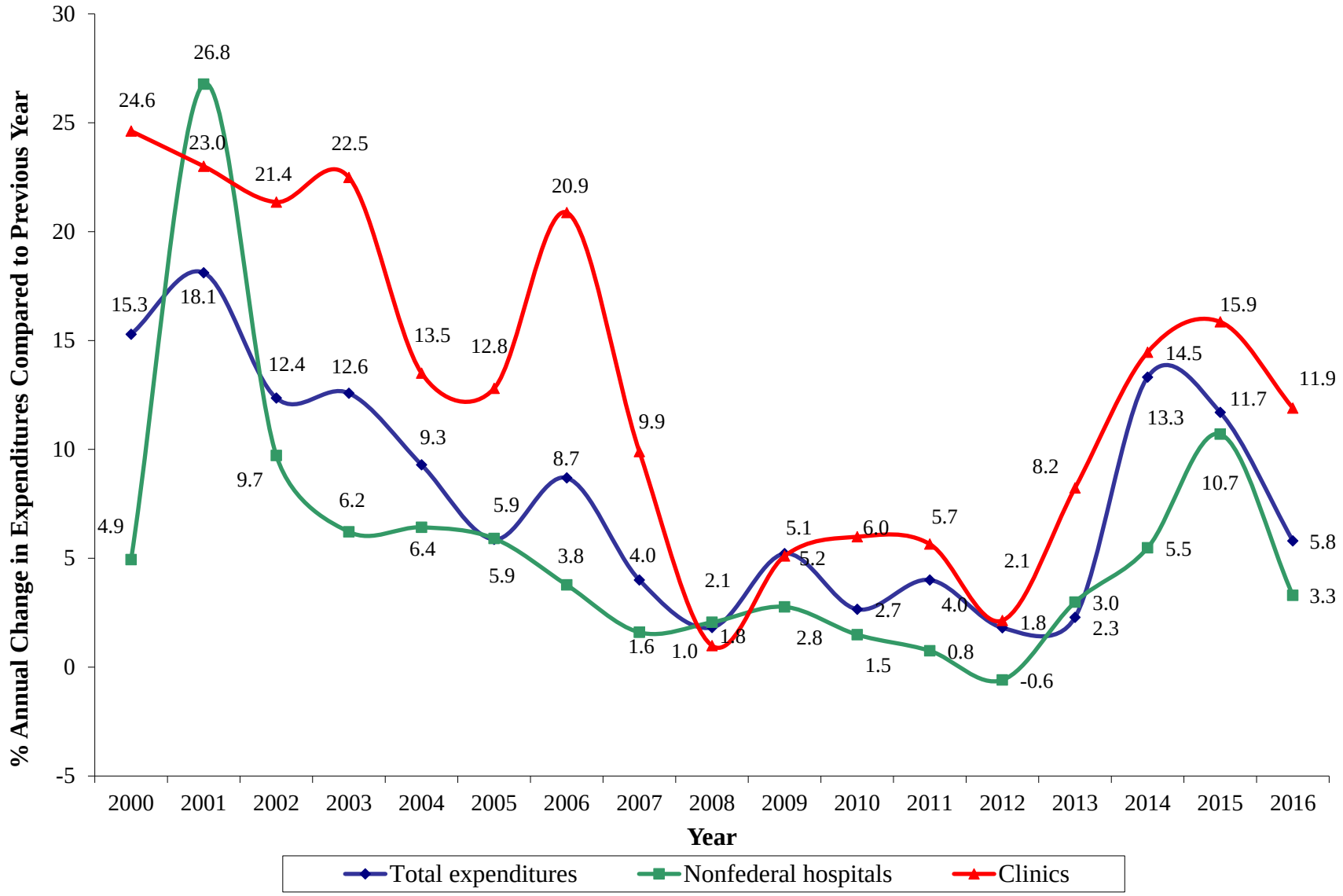
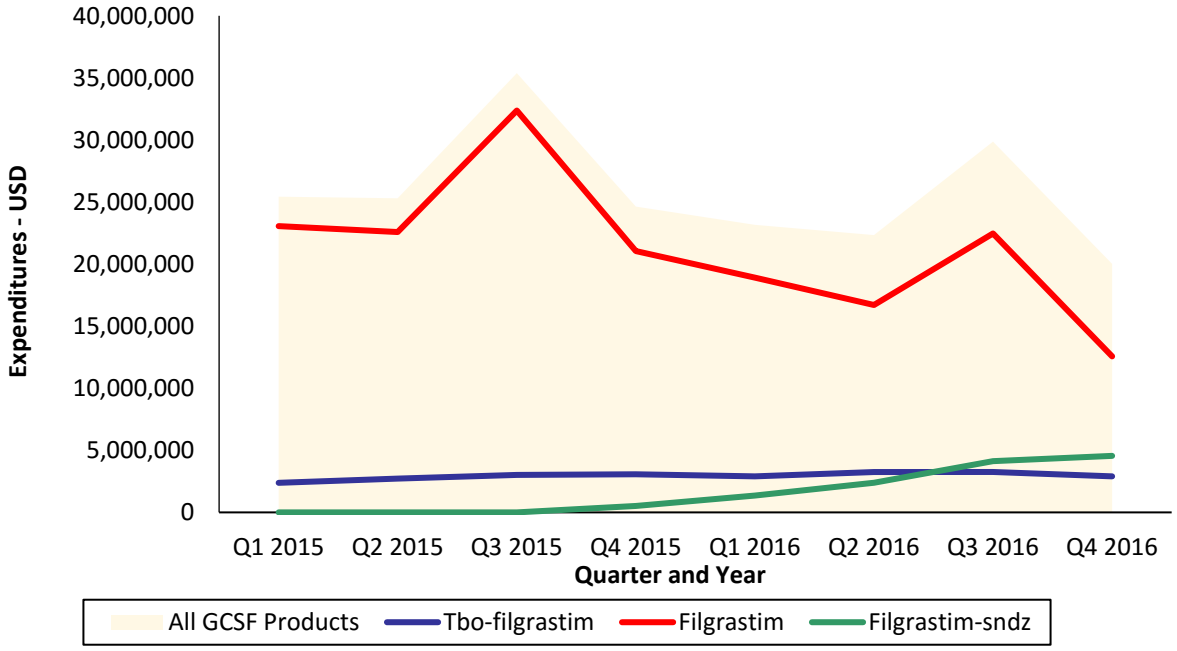


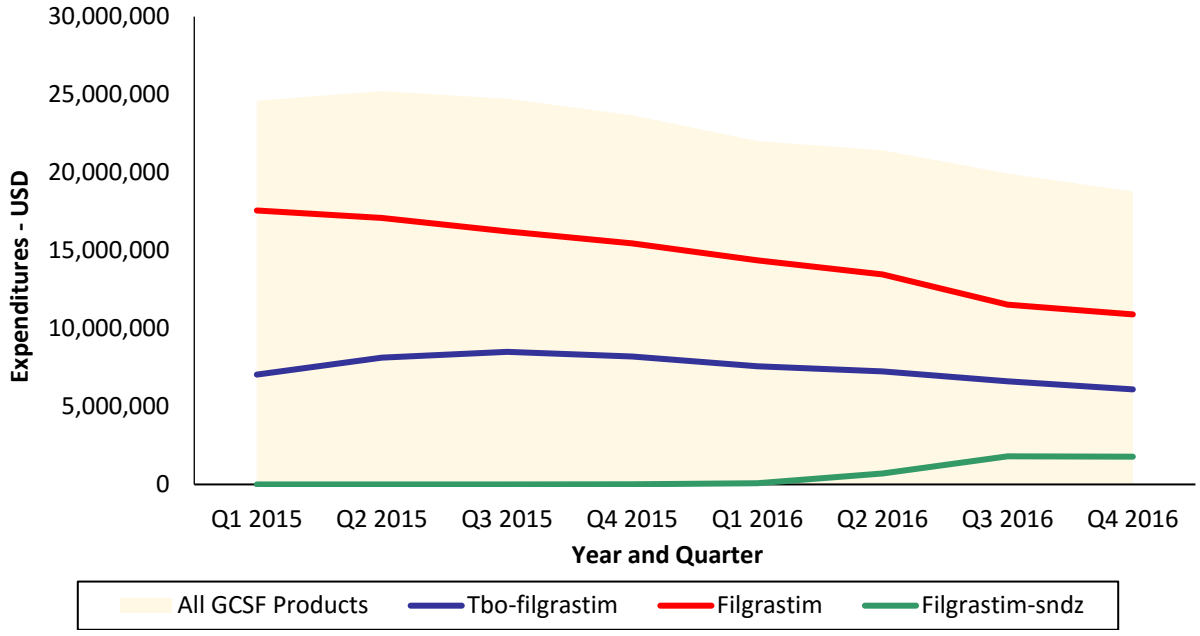
Figure 2. Expenditures GCSF products in clinics and non-federal hospitals in 2015 and 2016.

(A) GSCF Expenditures in Clinics



Abbreviations: GCSF = granulocyte-colony stimulating factors

(B) GSCF expenditures in nonfederal hospitals



Abbreviations: GCSF = granulocyte-colony stimulating factors

Table 1. Prescription Drug Expenditures and Growth by Sector in 2016

Sector[a]	**2016 Expenditures ($ Millions)**	**Percent of Total Expenditures**	**Percent Change from 2015**
Retail pharmacies	217,428	48.5	4.7
Mail-order pharmacies	103,171	23.0	6.7
Clinics	63,693	14.2	11.9
Nonfederal hospitals	34,461	7.7	3.3
Long-term care	16,541	3.7	0.3
Health maintenance organizations	5,084	1.1	6.5
Home health care	3,672	0.8	2.0
Federal facilities	2,890	0.6	7.9
Other	1,232	0.3	8.4
Total	448,173		5.8

Footnotes

[a] Definitions of sectors shown in table are provided 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).

Table 2. Factors Driving Growth of Pharmaceutical Expenditures in Clinics and Nonfederal Hospitals in 2016, by Product Category[a]

	Clinics				Nonfederal Hospitals			
	Total Percent Growth	Percent Growth Due to Factor			Total Percent Growth	Percent Growth Due to Factor		
Product Category		New Products	Price	Volume and mix		New Products	Price	Volume and mix
All products	11.9	1.9	1.9	8.1	3.3	1.6	4.6	-3.0
Injectables	12.4	1.5	2.4	8.5	4.0	1.5	4.4	-2.0
Brands	12.0	1.4	2.9	7.7	2.4	1.2	4.4	-3.3
Generics	7.3	3.7	-5.3	8.9	6.3	3.7	1.3	1.2
Branded generics	21.5	0.2	3.6	17.7	8.7	0.7	7.8	0.2
Noninjectables	10.2	3.5	0.2	6.5	1.3	2.0	5.2	-5.9
Brands	12.4	2.8	2.4	7.2	0.5	2.0	9.3	-10.8
Generics	1.0	8.5	-12.4	4.9	0.6	3.9	-2.6	-0.7
Branded generics	7.5	0.4	3.2	3.9	3.0	0.1	4.8	-1.8

Footnotes

[a] Total growth is comprised of three factors/elements, these include: 1) new products - which 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; 2) price – which represents growth in expenditures due 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); and 3) volume and mix – which refers to growth in expenditures caused by either changes in volume of

utilization of existing products or changes in utilization patterns (i.e., from one product to another, for example when prescribing moves from brand to generic products).

Table 3. Top 25 Drugs by Expenditures Overall in 2016		
Drug[a]	**2016 Expenditures ($ Thousands)**	**Percent Change from 2015**
Adalimumab	13,590,435	27.6
Insulin glargine	10,063,158	2.6
Ledipasvir sofosbuvir	9,959,780	-30.1
Etanercept	7,362,086	11.2
Infliximab	5,309,916	6.6
Fluticasone salmeterol	5,227,906	0.4
Insulin lispro	5,108,684	28.3
Insulin aspart	4,964,540	10.2
Rosuvastatin	4,943,624	-20.9
Sitagliptin	4,787,767	15.1
Pregabalin	4,395,804	15.0
Glatiramer	4,274,347	-4.6
Pegfilgrastim	4,237,673	3.2
Rituximab	3,913,944	6.6
Insulin detemir	3,730,934	0.4
Dimethyl fumarate	3,666,714	6.0
Rivaroxaban	3,589,899	27.2
Emtricitabine tenofovir disoproxil	3,400,820	23.0
Tiotropium bromide	3,366,359	-5.7
Apixaban	3,167,756	98.0
Lisdexamfetamine	3,111,569	18.2

Bevacizumab	3,082,273	-1.8
Budesonide formoterol	3,035,857	13.2
Trastuzumab	2,655,434	5.5
Nivolumab	2,649,364	246.2

Footnote

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

Table 4. Top 25 Drugs by Expenditures in Clinics in 2016		
Drug[a]	**2016 Expenditures ($ Thousands)**	**Percent Change From 2015**
Infliximab	3,461,368	5.5
Pegfilgrastim	3,137,053	5.7
Rituximab	2,695,633	7.6
Bevacizumab	2,421,040	1.4
Trastuzumab	2,096,180	9.1
Nivolumab	2,075,405	258.1
Erythropoietin alpha	1,809,605	-26.4
Denosumab	1,608,782	19.6
Ranibizumab	1,399,783	-8.1
Pneumococcal vaccine	1,348,890	-17.4
Immune globulin	1,139,961	33.3
Pemetrexed	895,745	-5.5
Sevelamer	864,646	5.9
Influenza virus vaccine	857,171	9.5
Darbepoetin alfa	847,388	31.3
Human papillomavirus vaccine	766,975	24.5
Pertuzumab	747,562	15.5
Natalizumab	714,334	9.3
Ledipasvir sofosbuvir	659,762	-28.7
Abatacept	655,941	21.4
Ipilimumab	652,210	37.8

Vaccine varicella	632,281	-1.5
Pembrolizumab	561,606	104.7
Octreotide	555,725	0.8
Paclitaxel	546,302	-7.7

Footnote

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

Table 5.

Top 25 Drugs by Expenditures in Nonfederal Hospitals in 2016

Drug[a]	2016 Expenditures ($ Thousands)	Percent Change[b]
Infliximab	1,093,296	4.9
Rituximab	1,042,140	3.9
Immune globulin	904,531	9.2
Pegfilgrastim	822,185	-3.1
Alteplase	795,168	9.0
Natalizumab	738,005	4.7
Bevacizumab	544,818	-11.8
Nivolumab	511,128	221.4
Daptomycin	493,155	-4.9
Trastuzumab	489,865	-3.7
Piperacillin-tazobactam	469,313	6.5
Influenza virus vaccine	421,187	16.2
Pneumococcal virus	417,787	-14.1
Denosumab	336,370	13.0
Erythropoietin alpha	321,627	-1.1
Albumin	316,638	18.9
Regadenoson	300,239	0.5
Vasopressin	267,926	109.9
Filgrastim	265,598	-16.5
Iohexol	245,027	13.2

Enoxaparin	226,445	-19.3
Acetaminophen (i.v. only)	225,429	3.5
Darbepotin alfa	219,316	0.2
Bupivacaine	217,796	3.0
Iopamidol	217,694	25.6

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.

Table 6. Top 25 Therapeutic Drug Category by Expenditures in Nonfederal Hospitals in 2016

Drug Category	2016 Expenditures ($ Thousands)	Percent of Total 2016 Expenditures	Percent Change from 2015
Antineoplastic agents	6,079,079	17.5	4.3
Hemostatic modifiers	3,120,903	9.0	0.5
Antiinfectives, systemic	2,385,436	6.9	-8.1
Blood factors	1,975,376	5.7	-2.6
Biologicals	1,914,132	5.5	3.5
Gastrointestinal	1,851,622	5.3	2.1
Immunologic agents	1,705,287	4.9	14.1
Hospital solutions	1,384,243	4.0	14.3
Antiviral drugs	1,344,857	3.9	4.2
Respiratory therapy agents	1,171,358	3.4	4.7
Anesthetics	1,128,455	3.2	2.7
Diagnostic aids	1,092,851	3.1	8.9
Miscellaneous	1,075,601	3.1	7.7
Hormones	799,660	2.3	30.5
Analgesics	765,612	2.2	-4.8
Psychotherapeutics	739,955	2.1	-7.3
Musculoskeletal	674,207	1.9	13.6
Vascular agents	585,341	1.7	-3.4
Antiarthritics	579,999	1.7	23.7
Cardiac agents	561,651	1.6	3.4

Commented [SGT1]: "Antibacterials"?

Neurological disorder drugs	541,338	1.6	4.6
Diabetes therapy	424,914	1.2	4.6
Antifungal agents	377,206	1.1	1.7
Ophthalmic preparations	356,836	1.0	-2.5
Enzymes	353,875	1.0	5.0

Table 7. Selected Drugs and Biologicals That Have or May Receive FDA-Approved Labeling in 2017[a]				
Drug or Biological	**Manufacturer**	**Indication**	**Route**	**PDUFA Date[b] (Quarter)**
Telotristat etiprate	Lexicon Pharmaceuticals, Inc.	Carcinoid syndrome	Oral	Q1
Dupilumab	Regeneron Pharmaceuticals, Inc.	Moderate-to-severe atopic dermatitis	SC	Q1
Ocrelizumab	Genentech	Relapsing and primary progressive multiple sclerosis	IV	Q1
Abaloparatide	Radius Health, Inc.	Postmenopausal osteoporosis	SC	Q1
Valbenazine	Neurocrine Biosciences, Inc.	Tardive dyskinesia	Oral	Q2
Baricitinib	Eli Lilly and Company	Moderate to severe rheumatoid arthritis	Oral	Q2
Cerliponase alfa	BioMarin Pharmaceutical Inc.	Classic late infantile neuronal ceroid lipofuscinosis	IC	Q2
Brigatinib	ARIAD Pharmaceuticals, Inc.	Non-small cell lung cancer	Oral	Q2

Ribociclib	Novartis	Advanced breast cancer	Oral	Q2
17β-estradiol	TherapeuticsMD, Inc.	Dyspareunia in postmenopausal women with vulvar and vaginal atrophy	VAG	Q2
Midostaurin	Novartis	Adult acute myeloid leukemia	Oral	Q2
Nonacog beta pegol (long-acting factor IX)	Novo Nordisk	Haemophilia B	IV	Q2
Avelumab	EMD Serono Inc. and Pfizer Inc.	Merkel cell carcinoma	IV	Q2
Durvalumab	AstraZeneca	Urothelial carcinoma	IV	Q2
Edaravone	Mitsubishi Tanabe Pharma Corporation	Amyotrophic lateral sclerosis	IV	Q2
Methylphenidate extended-release orally disintegrating tablet	Neos Therapeutics, Inc.	Attention-deficit hyperactivity disorder	Oral	Q2
Binimetinib	Array BioPharma Inc.	Melanoma	Oral	Q2

Niraparib	TESARO, Inc.	Epithelial ovarian, fallopian tube, or primary peritoneal cancer	Oral	Q2
Romosozumab	Amgen and UCB	Osteoporosis	SC	Q3
Neratinib	Puma Biotechnology, Inc.	Extended adjuvant treatment (post-trastuzumab) in early stage breast cancer	Oral	Q3
Belimumab	GlaxoSmithKline	Autoantibody-positive systemic lupus erythematosus	SC	Q3
Glecaprevir-pibrentasvir	Enanta Pharmaceuticals, Inc.	Chronic hepatitis C virus, all major genotypes	Oral	Q3
Voxilaprevir-velpatasvir-sofosbuvir	Gilead Sciences, Inc.	Direct-acting antiviral-experienced chronic hepatitis C virus	Oral	Q3
Amantadine extended-release	Adamas Pharmaceuticals, Inc.	Levodopa-induced dyskinesia in patients with Parkinson's disease	Oral	Q3

Human anti-rabies immunoglobulin	Kedrion Biopharma, and Kamada Ltd.	Post-exposure treatment of rabies	IM	Q3
Amphetamine extended-release liquid suspension	Neos Therapeutics, Inc.	Attention-deficit hyperactivity disorder	Oral	Q3
Fluticasone furoate-umeclidinium-vilanterol	GlaxoSmithKline	Chronic obstructive pulmonary disease	INH	Q3
Sirukumab	Janssen Biotech, Inc.	Moderately to severely active rheumatoid arthritis	SC	Q3
FX006	Flexion Therapeutics, Inc.	Osteoarthritis of the knee	IA	Q4
Non-live, recombinant vaccine herpes zoster	GlaxoSmithKline	Prevention of herpes zoster	IM	Q4
Guselkumab	Janssen Biotech, Inc.	Moderate to severe plaque psoriasis	SC	Q4
Semaglutide	Novo Nordisk	Adults with type 2 diabetes	SC	Q4

Footnotes

[a] FDA = Food and Drug Administration, IA = intra-articular, IC = intracerebral, IM = intramuscular, INH = inhalation, IV = intravenous, PDUFA = prescription drug user fee act, Q = quarter, SC = subcutaneous, VAG = vaginally

[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 8. Selected Potential Patent Expirations for 2017.		
Drug	**Brand Name**	**Indication**
Atazanavir	Reyataz	Antiretroviral
Atomoxetine	Strattera	Attention deficit/hyperactivity disorder
Atovaquone	Mepron	Antiprotozoal
Bortezomib	Velcade	Antineoplastic
Buprenorphine	Butrans	Pain
Carglumic acid	Carbaglu	Endocrine Disorders
Caspofungin acetate	Cancidas	Antifungal
Ciclesonide	Omnaris	Allergies
Corticotropin	Acthar Gel	Endocrine Disorders
Eletriptan hydrobromide	Relpax	Antimigraines
Ertapenem	Invanz	Antimicrobial
Ezetimibe-simvastatin	Vytorin	Hypercholesterolemia
Iloperidone	Fanapt	Antipsychotic
Lovastatin	Altoprev	Hypercholesterolemia
Nelarabine	Arranon	Antineoplastic
Nitazoxanide	Alinia	Antiprotozoal
Octreotide acetate	Sandostatin LAR Depot	Endocrine Disorders
Pegaptanib sodium	Macugen	Age-related macular degeneration
Pegvisomant	Somavert	Endocrine Disorders
Rasagiline mesylate	Azilect	Parkison's Disease

Sumatriptan-naproxen sodium	Treximet	Antimigraines
Testosterone	Axiron	Hormonal Supplement
Vigabatrin	Sabril	Seizures
Zolpidem	Zolpimist	Sleep Disorders

Table 9. Top 15 Older Agents with High Growth in Expenditures within the Non-Federal Hospital and Clinic Channels in 2016.

Drug[a]	**2016 Expenditures ($ Thousands)**	**Percent Change From 2015**
Pyrimethamine	10,103	552.7
Thiotepa	39,570	394.3
Zinc sulfate	1,774	327.0
Tetrabenazine	2,849	303.6
Physostigmine salicylate	1,801	240.2
Chlodiazepoxide	2,529	168.5
Sodium bicarbonate	27,310	143.9
Phentolamine	9,034	109.4
Fluphenazine	8,656	107.5
Vasopressin	319,113	102.9
Indocyanine green	5,923	63.8
Lidocaine viscous	3,690	60.3
Calcitonin-salmon	114,880	58.6
Penicillamine	5,741	56.0
Albendazole	11,721	50.0

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.