

April 2016

Medicines Use and Spending in the U.S.

A Review of 2015 and Outlook to 2020



Introduction

Growth in spending on medicines for 2015, while slightly lower than 2014, continued at the highest levels since 2001, even as the future outlook suggests moderating growth through 2020. The challenges of balancing access and the cost of care in an era of innovative but more expensive treatments continue as a theme across our healthcare system.

In this report, we highlight different aspects regarding the use of medicines spanning overall spending, key market segments, volumes, patient cost exposure, healthcare delivery changes as well as the outlook to 2020.

Fueled by health reform initiatives and broader industry dynamics, the U.S. healthcare system remains in a state of flux impacting all stakeholders across the spectrum of healthcare - including patients. The goal of this report is to provide some context and perspective around the complex factors that determine the level of spending on medicines and their role in our healthcare system.

The study was produced independently by the IMS Institute for Healthcare Informatics as a public service, without industry or government funding. The contributions to this report of Kim Pennente, Michael Kleinrock, Jennifer Lyle, Lauren Caskey, Deanna Nass, Bernie Gardocki, Terri Wallace and dozens of others at IMS Health are gratefully acknowledged.

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Contents

01	Executive summary
06	Total spending on medicines
08	Drivers of growth
13	Major market segments
18	New medicines
25	Prescription volume
27	Patient cost exposure
31	Healthcare delivery changes
35	Outlook to 2020
38	Notes on Sources
40	Appendix
47	Authors
49	About the Institute

Executive summary

Spending on medicines increased by double digits for a second year in 2015 and reached \$425 billion based on invoice prices. After adjusting for estimated rebates and other price concessions by manufacturers, which rose sharply in 2015, net spending was \$310 billion, up 8.5% over 2014 levels. The surge of new medicines remained strong and the use of recently launched brands remained at historically high levels, while the savings from brands facing generic competition were relatively low. Specialty drug spending reached \$151 billion, up more than 20% from 2014.

Longer-term trends driven in part by the Affordable Care Act and in response to rising overall healthcare costs continued to play out in 2015. In particular, healthcare is being delivered by different types of healthcare professionals and in different facilities, and patients face higher out-of-pocket costs as well as access barriers.

The outlook for medicine spending through 2020 is for mid-single digit growth driven by further clusters of innovative treatments, offset by a rising impact from brands facing generic or biosimilar competition.

A Note on Nomenclature

In this report, “spending on medicines” and “invoice price spending” refer to the amounts paid to distributors by their pharmacy or hospital customers. It does not relate directly to either the out-of-pocket costs paid by a patient or the amount health plans pay for the medicines, and does not include mark-ups and additional costs associated with dispensing or other services associated with medicines reaching patients.

“Net price spending” is an alternative measure that is an estimate of the amount received by pharmaceutical manufacturers and therefore reflects rebates, off-invoice discounts and other price concessions made by manufacturers to distributors, health plans and intermediaries.

Total spending on medicines

Total spending on an invoice price basis reached \$424.8 billion in 2015, up 12.2% from 2014. Spending adjusted for net prices reached \$309.5 billion and grew by 8.5% over 2014. The growth rate moderated about 2% from the 2014 level, which was the highest since 2001 (see Chart 1).

The increase in spending in 2015 of \$46.2 billion on an invoice basis and \$24.3 billion on a net basis was driven by new brands and protected brand price increases, offset by the impact of patent expiries. Greater use of generics and a small increase in brand volume also contributed to growth (see Chart 2).

Drivers of growth

The average net price for brands already in the market is estimated to have increased by 2.8% in 2015, down from 5.1% in 2014 and significantly lower than seen in prior years. This reflects the heightened competition among manufacturers and more aggressive efforts by health plans and pharmacy benefit managers to limit price growth. Invoice price levels, prior to the impact of concessions, increased 12.4% in 2015, also down from the 2014 level (see Chart 3).

Offsetting other growth elements is the impact of new competition for brands resulting from the expiry of patents or other forms of market exclusivity. Spending on such brands fell by \$14.2 billion in 2015, a higher impact than in 2014, but much lower than the landmark year of 2012 when the comparable impact was \$32.6 billion (see Chart 4).

Over half of the total spending growth in 2015 was from new brands that have been available for less than 24 months. Patients are seeking and receiving new treatments for hepatitis, cancer, diabetes, and other chronic conditions, driving \$24.2 billion of new spending growth, slightly higher than in the prior year and significantly higher than historical levels (see Chart 5).

Spending on all generic medicines contributed \$7.9 billion to growth in 2015. Branded generics – those non-original medicines marketed with trade names – grew sharply on an invoice price basis, though some of this may have been offset by price concessions. The spike in invoice price increases of older generics seen in 2013 and 2014 is no longer driving growth in 2015 (see Chart 6).

Greater use of protected branded medicines contributed a modest \$2.7 billion to growth in 2015 but this is notable since in prior years, this element has had a negative impact on growth. The medicines contributing the most to volume growth were autoimmune and cancer treatments as well as anticoagulants (see Chart 7).

Major market segments

Those medicines classified by IMS Health as “specialty” contributed \$150.8 billion to the total spending on medicines in 2015, an increase of 21.5% over 2014, on an invoice price basis.

With more specialty treatment options becoming available and higher utilization, this remains one of the most dynamic segments of the total market (see Chart 8).

The surge of new and innovative treatments for patients with cancer continued in 2015 and contributed to rising expenditure on cancer therapeutics (excluding medicines used for supportive care) which reached \$39.1 billion, up 18.0% from 2014. The monoclonal antibodies segment accounts for 35% of the total and includes the remarkable new PD-1 inhibitors. Non-discounted spending on protein kinase inhibitors increased 27.1%, outpacing the 18.0% total oncology spending growth (see Chart 9).

The breakthrough hepatitis C treatments which have become available over the past two years were used to treat nearly 250,000 patients in 2015, up from 170,000 patients in the year prior and 20-30,000 per year in earlier periods. However, the number of new patient starts moderated as the year progressed, suggesting progress in working through the initial group of patients with the highest need (see Chart 10).

Multiple sclerosis treatments contributed \$17.7 billion to spending in 2015, with half of new therapy start patients leveraging the newer oral medicines now available (see Chart 11).

Growth in diabetes spending on an invoice price basis was \$10.1 billion in 2015, taking total spending to \$43.9 billion. However, off-invoice price concessions for existing and new brands – including the provision to patients of out-of-pocket cost assistance – are estimated to offset \$8-9 billion of this growth and are especially evident in the insulins segment (see Chart 12).

New medicines

A total of 43 New Active Substances (NAS) were launched in 2015, one-third of which had received an orphan drug designation from the FDA. An additional 30 brands were launched, not classified as NAS but bringing innovation in the form of combination therapies, alternative dosing, or treatment administration options. The strong momentum of research and development productivity and breakthroughs is reflected in these cohorts of new medicines, including the fourteen non-orphan NAS, with new mechanisms (see Chart 13).

Oncology medicines comprise the greatest share of launches by therapeutic area over the past 10 years, accounting for 35% of all launches in 2015 (see Chart 14). A growing number of additional indications are being granted to existing cancer medicines, with 10 such approvals in 2015 in addition to the 14 indications given to newly approved medicines (see Chart 15).

The uptake of the two innovative new medicines launched at the end of 2014 that target the immune system to fight cancer reflects their remarkable clinical success and expansion of indications (see Chart 16).

Among the NAS launches of 2015 were notable advances in precision medicines, rare disease treatments, and chronic disease medicines that could benefit large populations (see Chart 17). The additional 30 non-NAS brands that are based on existing medicines provide new treatments for orphan diseases, major efficacy improvements, and innovative administration (see Chart 18).

Significant advances occurred in 2015 for biosimilars, including the first approval under the biosimilar abbreviated pathway and subsequent launch, the submission to the FDA of seven biosimilar applications, and a growing number of biosimilar products advancing through clinical development (see Chart 19).

Prescription volume

Total prescriptions dispensed in 2015 reached 4,368 million, an increase of 1.0% which compares to increases of about 2 percent seen in earlier years. Notably, mail-order prescriptions declined in 2015 as off-patent medicines are increasingly filled as generics at retail pharmacies rather than being managed through mail order. Demand was higher in some therapy areas such as antidepressants and anti-diabetes which registered about 10% increases, while other areas declined including a notable 16.6% decline in the number of narcotic prescriptions dispensed (see Chart 20).

Provisions under the Affordable Care Act for coverage to the uninsured, through Medicaid Expansion and Health Exchange (HIX) plans, have been the leading driver of retail prescription growth in the past two years. At the same time, growth in Medicare Part D prescriptions has slowed, while the number of retail prescriptions filled through commercial plans (excluding HIX) and for cash have declined (see Chart 21).

Patient cost exposure

The average patient cost exposure for a brand prescription filled through a commercial plan has increased by more than 25% since 2010, reaching \$44 per prescription in 2015. Rising use of health plans with pharmacy deductibles, co-payments and co-insurance is contributing to this rise. The average patient cost exposure for generics, however, has remained at approximately \$8 since 2010 (see Chart 22).

In response to this rising level of patient cost exposure, brand manufacturers are steadily increasing their use of “buy-downs” through patient savings programs such as coupons or vouchers, to help patients offset these costs (see Chart 23). In the diabetes market, for example, coupons are being used to reduce the patient cost exposure in commercial plans, in particular for those patients facing \$50 or more per prescription. Of those patients, about half were able to reduce their out-of-pocket cost to zero in 2015 (see Chart 24).

Even after coupons are applied, patients with pharmacy deductible plans are still facing high cost exposure (see Chart 25).

Healthcare delivery changes

The growth of Integrated Delivery Networks (IDNs) with which healthcare professionals (HCPs) are affiliated, supports efforts by organizations to increase negotiating power with insurers, leverage economies of scale and drive pay for performance initiatives. Most states have seen an increased percentage of HCPs affiliated with IDNs since 2010 (see Chart 26).

Newer facility types addressing patient access and convenience, such as urgent care centers and pharmacy in-store clinics, have grown by 115% in the past five years, and are part of an increasingly diverse set of healthcare facilities (see Chart 27).

The number of prescriptions written by “non-physician practitioners” - Nurse Practitioners (NPs) and Physician Assistants - more than doubled over the past 5 years and reached 676 million prescriptions in 2015 (see Chart 28). Many states have expanded prescribing authority for NPs especially those with significant HCP shortage areas but some states prescribing remains restricted (see Chart 29).

Outlook to 2020

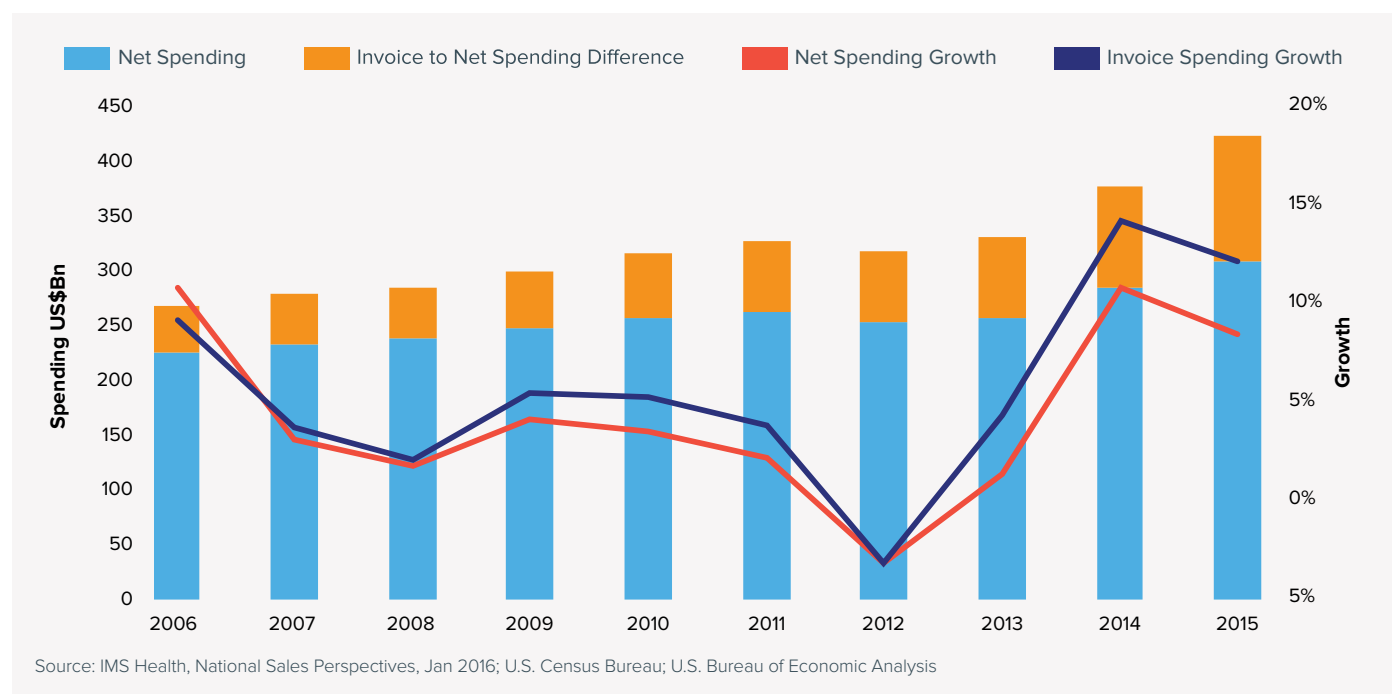
U.S. spending on medicines is forecast to reach \$610-640 billion in 2020 on an invoice price basis, with steady mid-single digit growth driven by innovation and offset by loss of exclusivity (see Chart 30).

Of the \$282 billion of growth over the next five years from branded medicines, \$91 billion is forecast to result from new medicines launched during that period, with the largest share coming from oncology. While brand price increases are expected to continue in the 10-12 percent range on an invoice basis, these will be significantly offset by rebates, discounts and other forms of price concessions (see Chart 33).

The prospects for further innovative medicines becoming available over the next five years are very bright. The late phase pipeline holds 2,320 novel products and 43-49 New Active Substances are expected to be launched on average for each of the next five years. Oncology remains the area of greatest research activity (see Chart 32).

Spending on medicines in 2015 increased 8.5% on a net basis to \$309.5Bn and 12.2% to \$424.8Bn on an invoice basis

Chart 1: Total Spending on Medicines US\$Bn



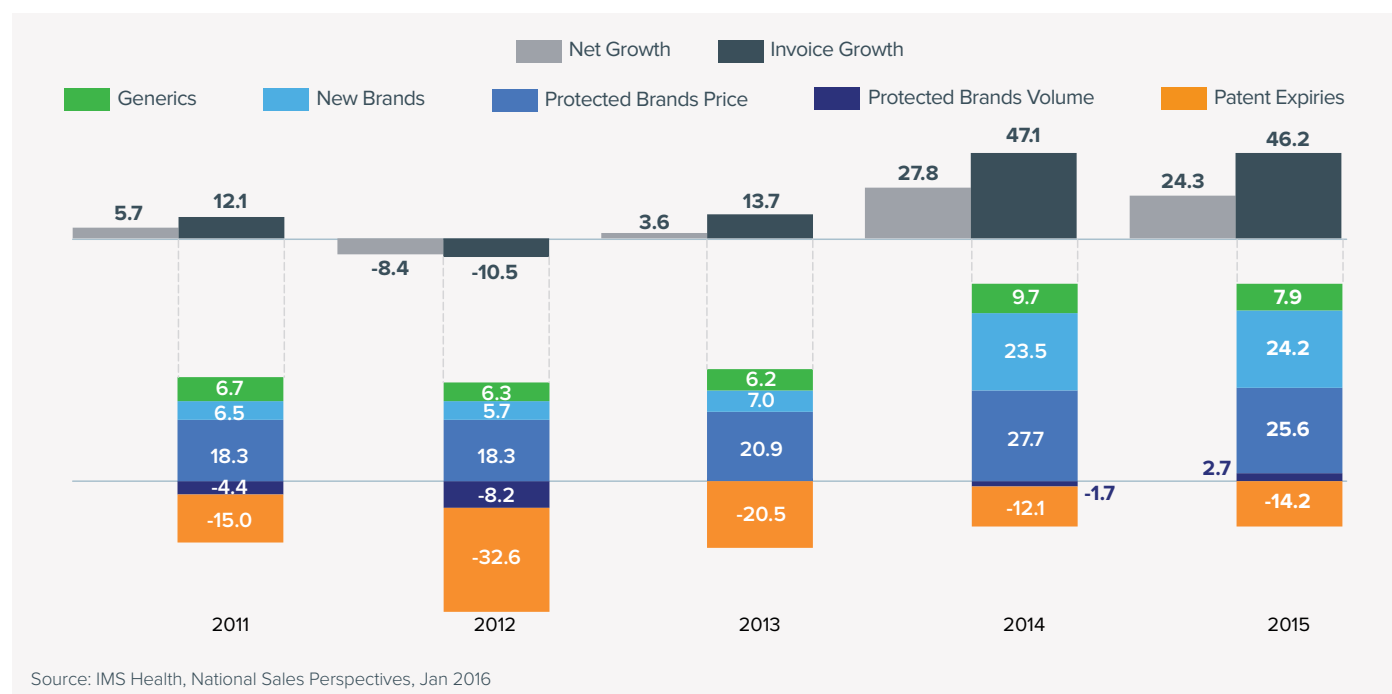
- Spending grew 8.5% net of off-invoice discounts and rebates, driven above the levels of the past ten years primarily by a wave of innovative new medicines.
- From 2006 to 2015, real per capita spending rose 26.9% from \$949 to \$1,204 on an invoice basis, but increased more slowly on a net basis, rising 9.5% from \$801 to \$877.
- Discounts, rebates and other price concessions on brands reduced absolute invoice spending by an estimated 27.1%.
- Spending growth was historically high for the second year in a row, but slowed by approximately 2% from 2014 on both an invoice and net basis.
- The biggest drivers of growth in 2014 – the uptake of innovative brands, the prices of protected brands, and a lack of major patent expiries – continued to drive growth in 2015.
- Some drivers of 2014 growth have moderated in 2015, such as brand invoice price increases, generic price growth, and the contribution from specific classes of innovative medicines such as hepatitis C.

Chart notes:

Measures total value of spending on prescription medicines and insulins by retail pharmacies, hospitals, and other institutional pharmacies at invoice prices. Invoice spending is based on IMS Health reported values from wholesaler transactions measured at trade/invoice prices and exclude off-invoice discounts and rebates that reduce net revenue received by manufacturers. Net spending reflects company recognized revenue after off-invoice discounts, rebates and price concessions are applied. Real Per capita adjustments based on data from U.S. Census Bureau and U.S. Bureau of Economic Analysis. Real per-capita spending reported in 2009 dollars.

The increase of \$24.3Bn in spending on a net basis and \$46.2Bn on an invoice basis has five major drivers

Chart 2: Spending Growth and Drivers US\$Bn



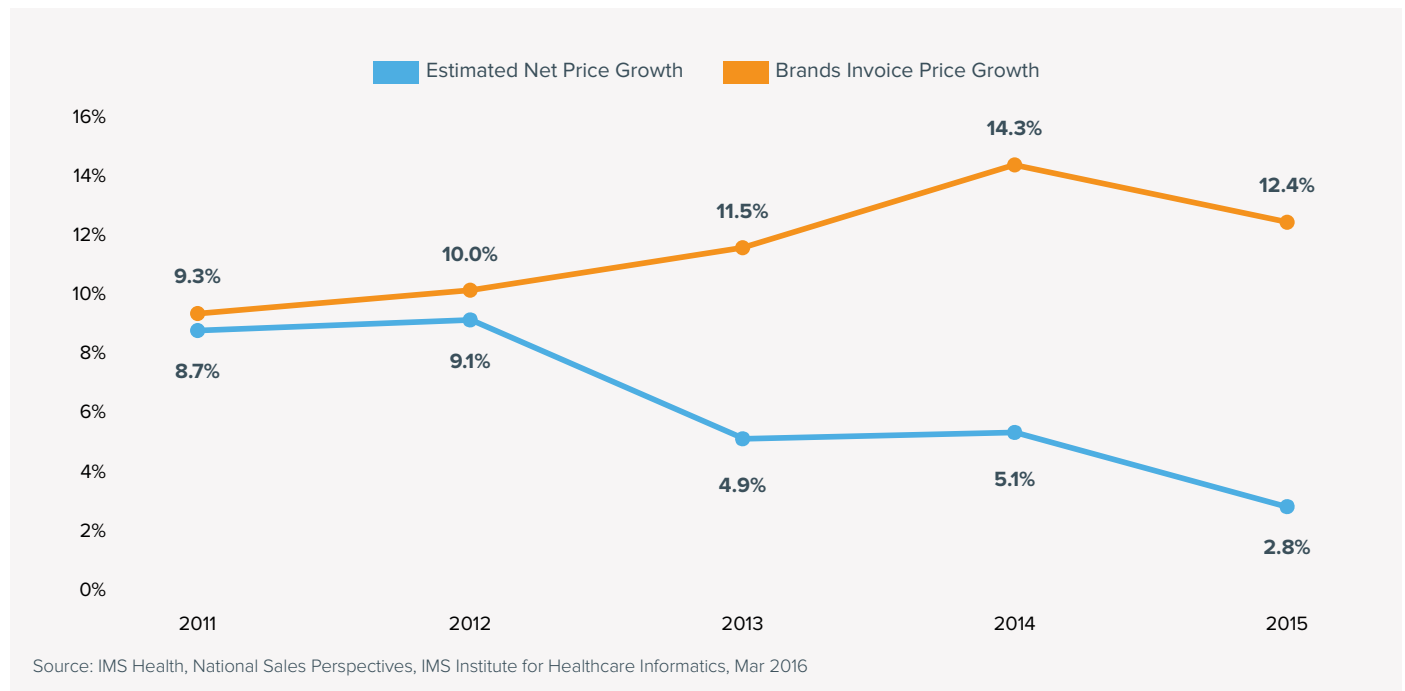
- On a net basis, total spending on medicines grew \$24.3Bn to \$309.5Bn in 2015, and \$46.2Bn on an invoice basis.
- Invoice spending on new brands increased \$24.2Bn in 2015, reflecting a second year of record new brand spending growth.
- Spending on protected brands increased \$28.3Bn in 2015, including both volume growth and price increases.
- Volume growth contributed \$2.7Bn to protected brand spending growth.
- Increases in the invoice prices of protected brands raised spending by \$25.6Bn, but an estimated \$20–22Bn in price concessions were given back, resulting in net protected brand price growth of \$4–6Bn.
- Recent patent expiry events resulted in a \$14.2Bn reduction in invoice spending.
- Generic spending increased \$7.9Bn in 2015.

Chart notes:

Stacked segments are mutually exclusive. Protected brand growth is split by volume and price. New brands segment includes products launched in the past twenty-four months. Patent expiry category shows the impact of lower spending on products that lost exclusivity. Invoice values are IMS Health reported values from wholesaler transactions measured at trade/invoice prices and exclude off-invoice discounts and rebates that reduce net revenue received by manufacturers. Net values denote company recognized revenue after discounts, rebates and other price concessions.

Net price growth slowed in 2015 to 2.8% as price concessions by manufacturers rose sharply

Chart 3: Protected Brand Invoice and Net Price Growth



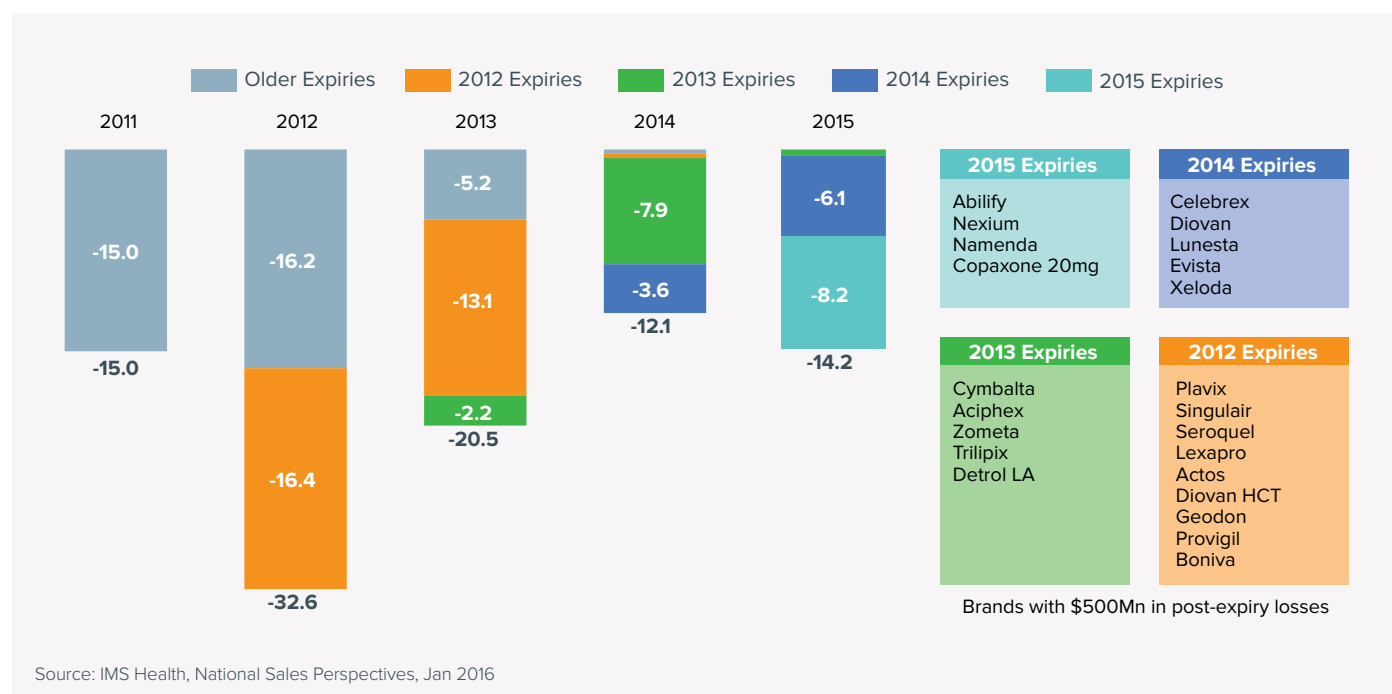
- Although price growth for protected brands was 12.4% on an invoice price basis, net price growth is estimated to have increased 2.8% in 2015 on average.
- Discounts, rebates and other price concessions offset protected brands price growth by an estimated 77–81% in 2015.
- Net protected brands price growth has slowed since 2012, with 2015 reflecting the smallest increase in recent years.
- Brand invoice price growth also slowed this year, declining from 14.3% in 2014.
- Price spending growth was offset by large net price declines in hepatitis, diabetes, and pain therapies, while price growth was driven by autoimmune, multiple sclerosis, and oncologic therapies.
- The widening gap between invoice price growth and net price growth reflects higher levels of off-invoice discounts, price protection, rebates and price concessions since 2013, which coincides with a period of higher levels of invoice price growth and intensified competition.

Chart notes:

Invoice values are IMS Health reported values from wholesaler transactions measured at trade/invoice prices and exclude off-invoice discounts and rebates that reduce net revenue received by manufacturers. Net values denote company recognized revenue after discounts, rebates and other price concessions. Results are based on a comparative analysis of company reported net sales and IMS Health audited sales and prices at product level for branded products representing 79–93% of brand spending in the period displayed. Growth rates are calculated over same cohort of products in the prior year.

Brand loss of exclusivity reduced spending by \$14.2Bn in 2015, slightly higher than the impact in the prior year

Chart 4: Decline in Brand Spending from Loss of Exclusivity US\$Bn



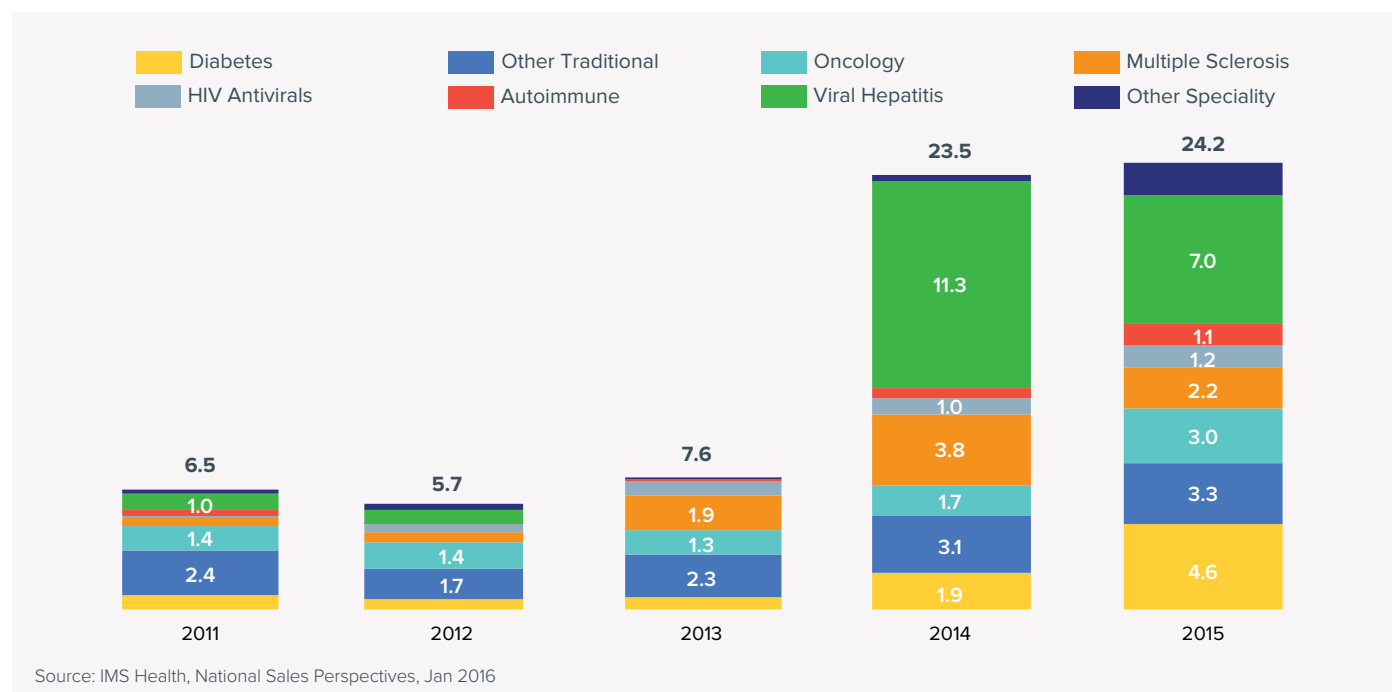
- Recent patent expiry events resulted in a \$14.2Bn reduction in brand spending in 2015.
- The biggest patent expiries for 2015 were Abilify, Nexium, and Namenda; oral therapies for common chronic conditions.
- Teva launched Copaxone 3-times-a-week (40mg) ahead of Sandoz's Glatopa, a substitutable glatiramer acetate 20mg for relapsing multiple sclerosis.
- The launch of generic celecoxib and valsartan in 2014 led to \$6.1Bn lower spending on the brands they replaced in 2015.
- The loss of exclusivity for three notable blockbuster brands – Suboxone, Neupogen, and Copaxone – did not result in significant declines in brand spending.

Chart notes:

Includes all branded medicines that have lost patent exclusivity and faced competition from generics or non-original biologics. Measures lower brand spending, not generic savings. Loss of exclusivity dates were determined using patent expiry dates and generic entry dates. Older expiries category includes all branded medicines that lost exclusivity prior to 2012.

Patient use of new treatments drove a historically high level of \$24.2Bn of growth in 2015

Chart 5: New Brand Spending Growth US\$Bn



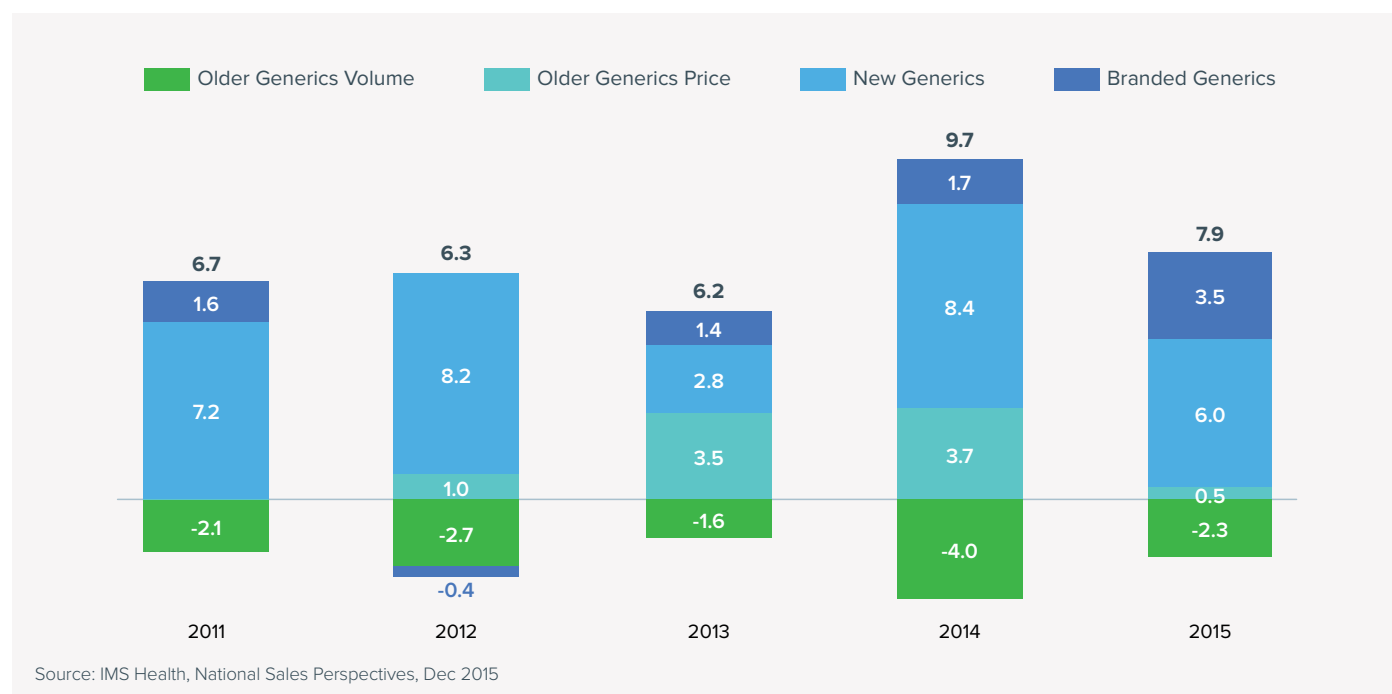
- Higher levels of new brand spending growth continued into 2015 as spending on new brands increased by \$24.2Bn to \$42.3Bn.
- Specialty medicines, a \$150.8Bn market, account for 36% of total spending and 75% of new brand spending growth.
- Hepatitis C drove new brand spending growth supported by new treatments, most notably the ledipasvir-sofosbuvir combination launched in late 2014.
- Other new specialty medicines driving growth include an easier dosing option for multiple sclerosis, a combination therapy for HIV, targeted immunotherapies for cancer, and new treatments for autoimmune conditions.
- Traditional medicines, a \$270Bn market, account for 64% of total spending but only 33% of new brand spending growth.
- Traditional medicines contributing to new brand growth include a new HPV vaccine, a new class of diabetes medicines known as SGLT2 inhibitors, and a treatment for toenail fungus.

Chart notes:

Spending based on invoice price and does not reflect off-invoice discounts and price concessions. New brands are defined as brands launched in the past twenty-four months. Specialty medicines are defined by IMS Health as products that are often injectable, high-cost, biologics or other medicines that require cold-chain distribution. Specialty medicines are mostly initiated by specialists, and include treatments for cancer and other chronic conditions. Specialty medicines often require complex patient follow-up and monitoring.

The contribution to growth of branded generics increased while that of older generics price moderated

Chart 6: Contribution to Generic Spending Growth US\$Bn



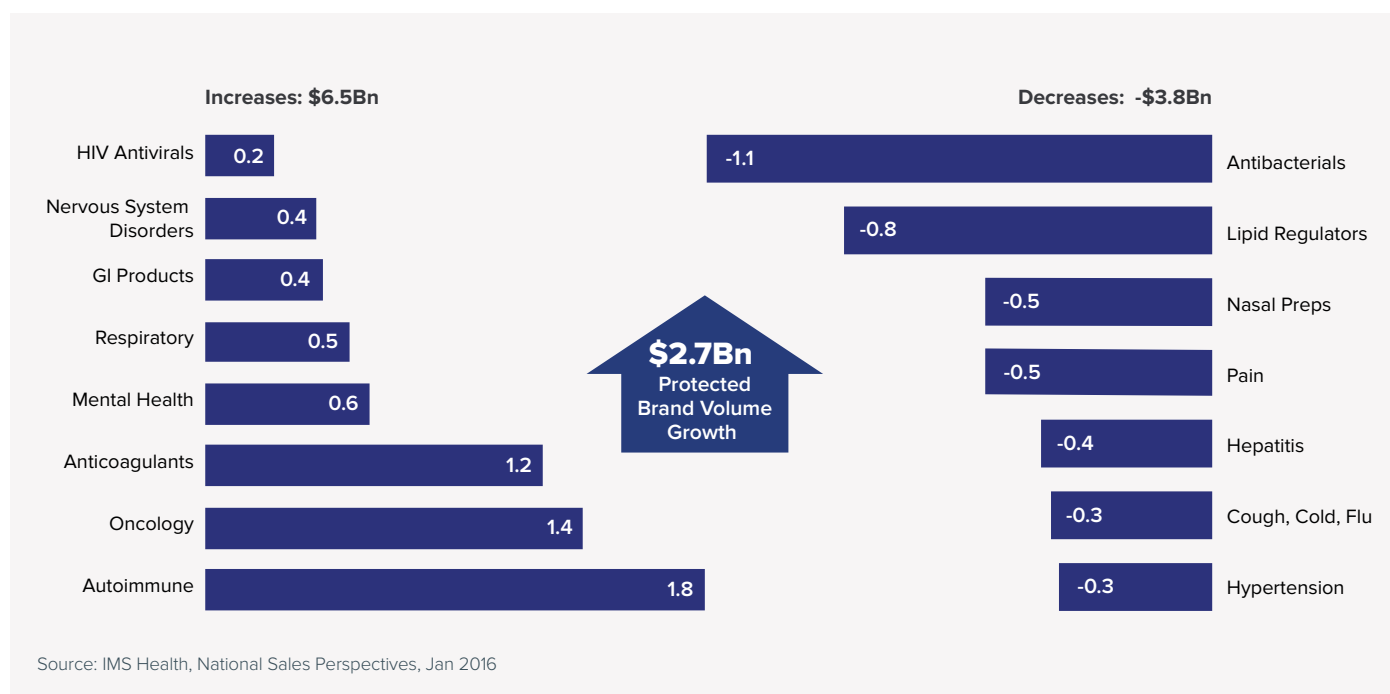
- Generic spending increased \$7.9Bn to \$114.1Bn in 2015, an increase of 7.4%.
- Branded generics accounted for 40% of generic spending and 45% of generic spending growth in 2015.
- The arrival of aripiprazole, esomeprazole, and celecoxib generics drove generic spending growth in 2015.
- Spending on single source generics accelerated in the past two years, but only accounted for 7% of generic sales and 19% of generic spending growth in 2015.
- In 2014, the leading drivers of generic growth were duloxetine, lidocaine, levothyroxine, valsartan, and oxycodone/apap.
- Prices increases for older generics moderated significantly in 2015, contributing only \$0.5Bn in growth in 2015 compared to over \$3.0Bn in the prior two years.
- Spending on older generics has decreased partly due to declining use of doxycycline, enoxaparin, modafinil, cyclophosphamide and omeprazole.

Chart notes:

Newer generics are unbranded generics that have launched in the past two years. Older generics include unbranded medicines that launched more than two years ago. Branded generics are defined by IMS Health as non-original medicines marketed with trade names, including Proair HFA, Restasis, Epipen, Androgel, Aderall XR, Rebif, Glumetza, and others.

Modest spending growth from greater use of existing branded drugs in 2015 marks a reversal of recent trends

Chart 7: Protected Brand Volume Change by Therapy Area US\$Bn



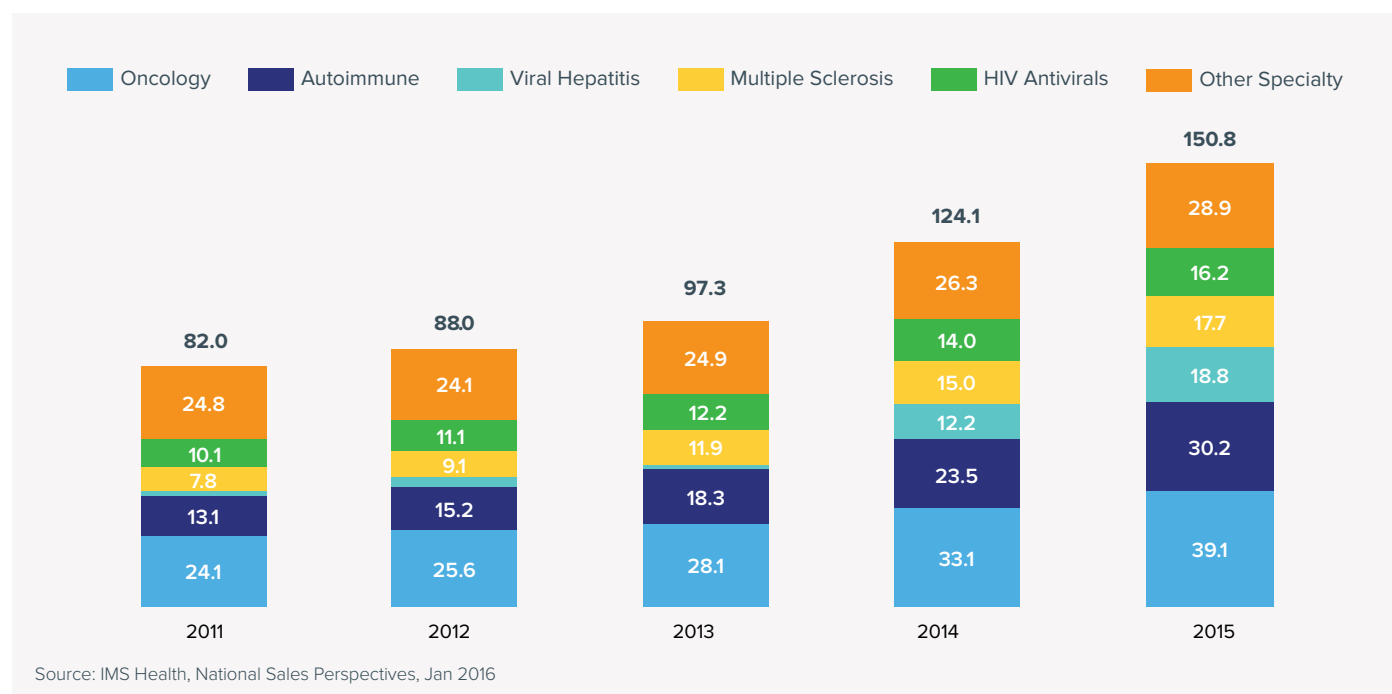
- Volume growth contributed \$2.7Bn of the total \$28.3Bn increase in spending on protected brands in 2015.
- This marks the first year since 2007 that volume was a positive driver of protected brand spending growth.
- Positive protected brand volume growth was driven by greater utilization of medicines for autoimmune conditions, cancer, blood clots, and mental health conditions.
- Lower utilization of antibacterials, lipid regulators, and prescription painkillers counterbalanced the overall protected brand volume growth.
- In therapy areas with declining protected brand volume, patients may have shifted to generics (lipid regulators, anti-ulcerants), or to newer brands (hepatitis).
- Protected brand volume declines could be a result of policy initiatives intended to encourage more responsible use of antibiotics and pain medications.

Chart notes:

The protected brand segment includes products that are over two years old and have not yet faced generic competition. Protected brand growth is split by volume and price in Chart 2; only the contribution from volume is shown here. This analysis does not separate mix change, or shifts to more or less expensive brands, from volume and price.

Spending on specialty medicines in 2015 increased 21.5% to \$150.8Bn on an invoice price basis

Chart 8: Spending on Specialty Medicines US\$Bn



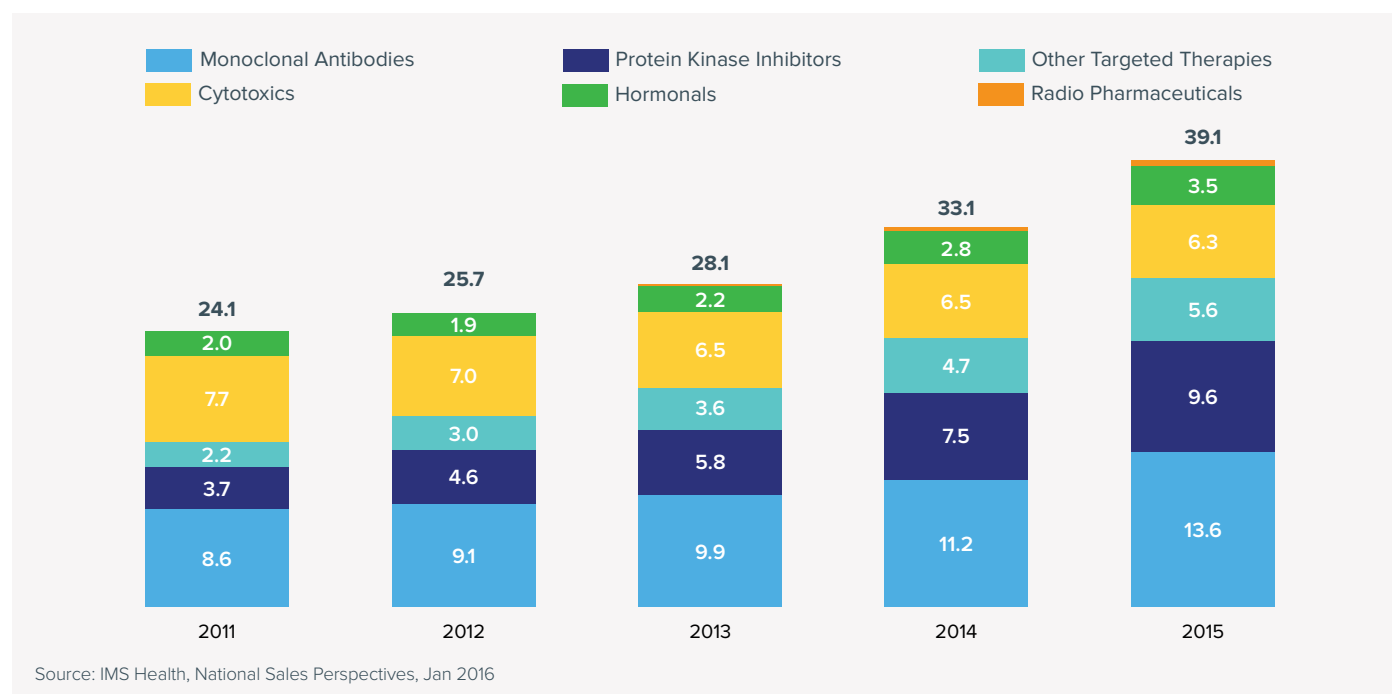
- Spending on specialty medicines doubled in the past five years, contributing 70% of overall medicine spending growth between 2010 and 2015.
- Specialty medicines now account for 36% of non-discounted medicine spending, up from 24% in 2010.
- Increased specialty spending was driven primarily by treatments for hepatitis, autoimmune diseases, and oncology which accounted for \$19.3Bn in increased spending.
- Specialty medicines spending increased on an invoice price basis by 21.5% to \$150.8Bn in 2015; specialty growth was 18.0% excluding hepatitis.
- Spending on treatments for viral hepatitis increased \$6.6Bn to \$18.8Bn in 2015.
- Oncology spending increased \$6.0Bn to \$39.1Bn in 2015, or 18.0%.
- Spending on treatments for autoimmune diseases rose 28.7% to \$30.2Bn on an invoice price basis, though discounts and rebates offset much of this increase.
- Multiple sclerosis spending increased \$2.6Bn or 17.6% to \$17.7Bn in 2015.
- Sales of HIV antivirals increased 15.7%.

Chart notes:

Specialty medicines are defined by IMS Health as products that are often injectable, high-cost, biologics, or require cold-chain distribution. They are often initiated by specialists, and include treatments for cancer and other chronic conditions. Specialty medicines often require complex patient follow-up and monitoring. Supportive care products are not included in the oncology market.

Oncology spending increased 18.0% to \$39.1Bn in 2015, driven by new breakthrough treatments for cancer patients

Chart 9: Spending on Oncology Medicines US\$Bn



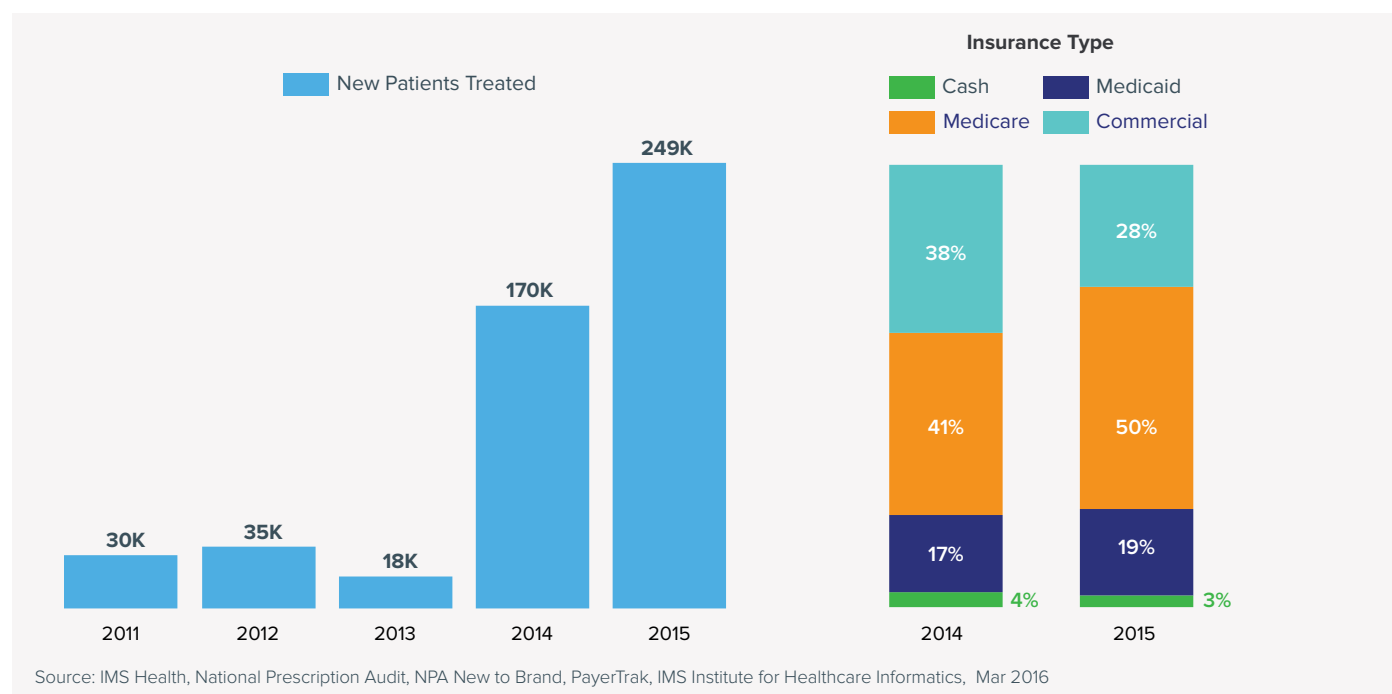
- Spending on oncology medicines increased 18.0%, or \$6.0Bn, to \$39.1Bn in 2015.
- The fastest growing classes within oncology are monoclonal antibodies and protein kinase inhibitors, both types of targeted therapies.
- Monoclonal antibodies (mAbs) account for 35% of oncology spending, with the increase in spending on mAbs is driven both by new innovative treatments (PD-1 inhibitors) and existing therapies.
- The uptake of two newer medicines, palbociclib and ibrutinib, helped drive spending on protein kinase inhibitors up 27.1% to \$9.6Bn in 2015.
- Two cancer treatments (capecitabine and bexarotene) became available as generics in the past two years, creating savings for patients and the health care system.
- Imatinib, the fourth highest selling cancer treatment in 2015, became available as a generic medicine in February 2016, and will bring about further cost savings.

Chart notes:

Oncology market defined as L1 antineoplastics, L2 cytostatic hormone therapies, V3C radio pharmaceuticals, denosumab, lenalidomide, pomalidomide, and aldesleukin. Supportive care is not included.

Nearly 250,000 new patients received treatment for hepatitis C in 2015

Chart 10: Patients Treated with Hepatitis Medicines



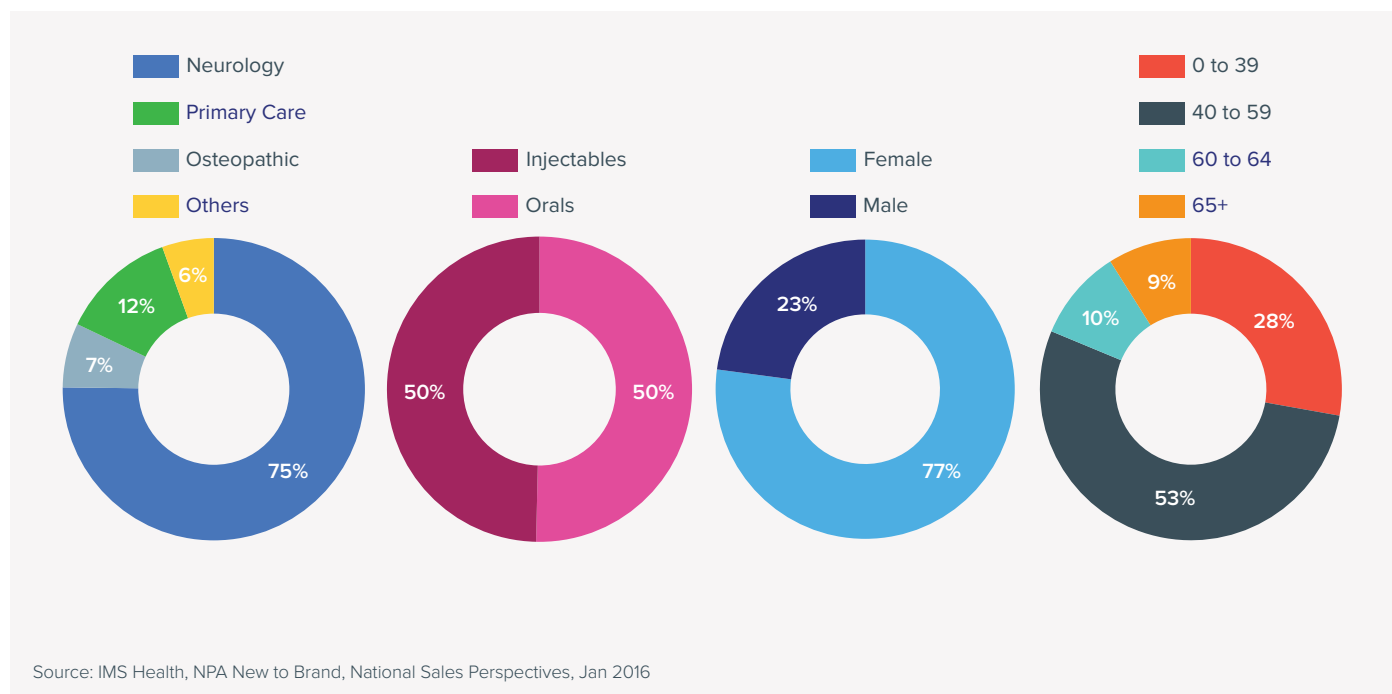
- Nearly 250,000 new patients received treatment for hepatitis C in 2015, a 46% increase from 2014.
- As a result of hepatitis C treatments offering cure rates of over 90% and fewer side effects, the past two years have seen 5 times the number of patients treated than in the prior three years.
- Patient new therapy starts peaked in March 2015 and have started to slow as the majority of patients most in need have sought and received treatment.
- The discussion continues over the price of these medicines and the criteria for determining patient access and insurance coverage.
- To date, over 400,000 patients have been treated with at least one of the six medicines launched in the past two years resulting in \$31.0Bn in non-discounted spending.
- For 2015, a higher percent of treatments were for Medicare and Medicaid patients and while the percent of Commercial patients declined they still accounted for over a quarter of patients treated.

Chart notes:

New patients are defined as new to brand prescriptions for Daklinza, Incivek, Victrelis, Sovaldi, Olysio, Harvoni, Technivie and Viekira Pak. Patient estimates are adjusted based on company reports and IMS Health estimates. Medicaid includes both fee for service and managed Medicaid. Commercial insurance includes exchange plans (HIX). Method of payment breakdown based on total retail prescriptions.

Multiple sclerosis treatments contributed \$17.7Bn to spending in 2015 with oral medicines now used in half of new therapy starts

Chart 11: Patients Treated with Multiple Sclerosis Medications



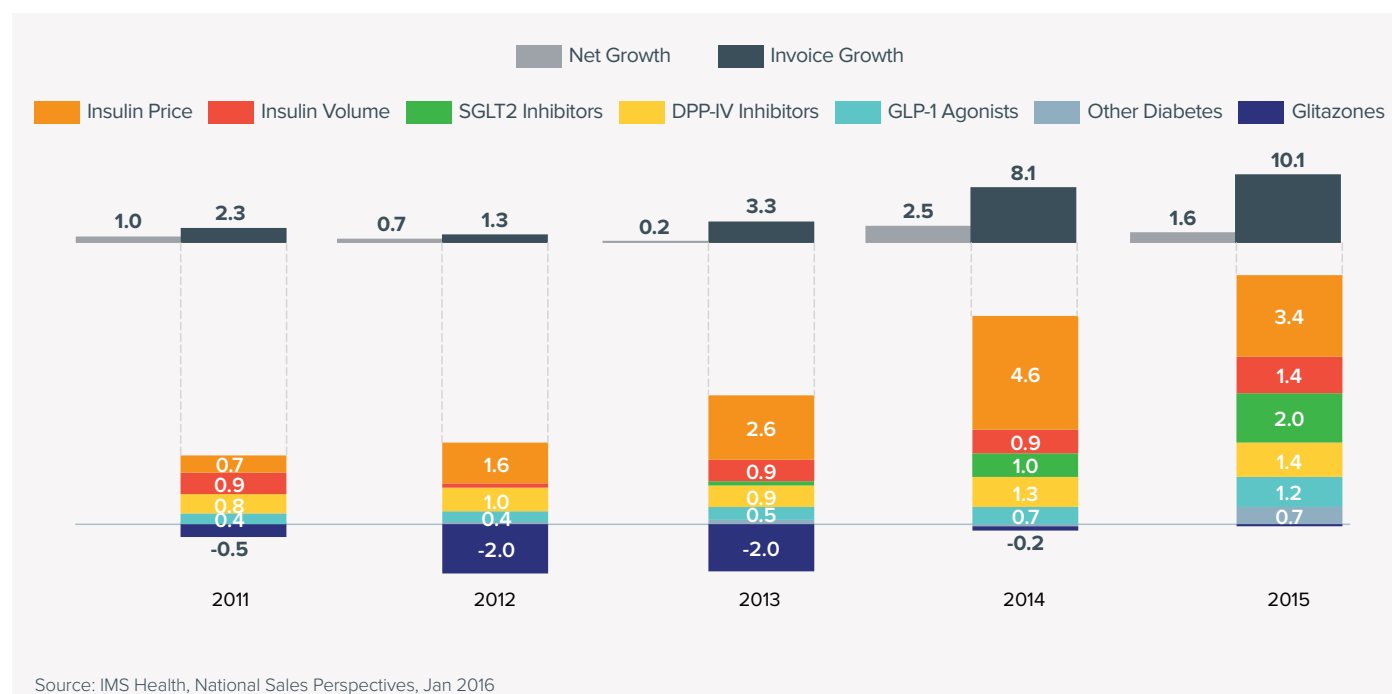
- Multiple sclerosis disproportionately affects women, many of whom begin treatment for this neurological disease after age forty.
- Over 70% of patients who began treatment for multiple sclerosis in 2015 were over 40 years old.
- Eighty-seven percent of prescriptions for newly diagnosed patients are written by referring primary care physicians or neurologists who often coordinate disease management.
- Oral medicines now account for half of new treatment starts in 2015, steadily increasing since the introduction of these new treatment options six years ago and up from 26% in 2011.

Chart notes:

Multiple sclerosis market is defined as interferons, dimethyl fumarate, fingolimod, glatiramer, natalizumab, and teriflunomide.

Growth in spending on diabetes medicines was \$10.1Bn on an invoice price basis but price concessions offset this significantly

Chart 12: Diabetes Spending Growth US\$Bn



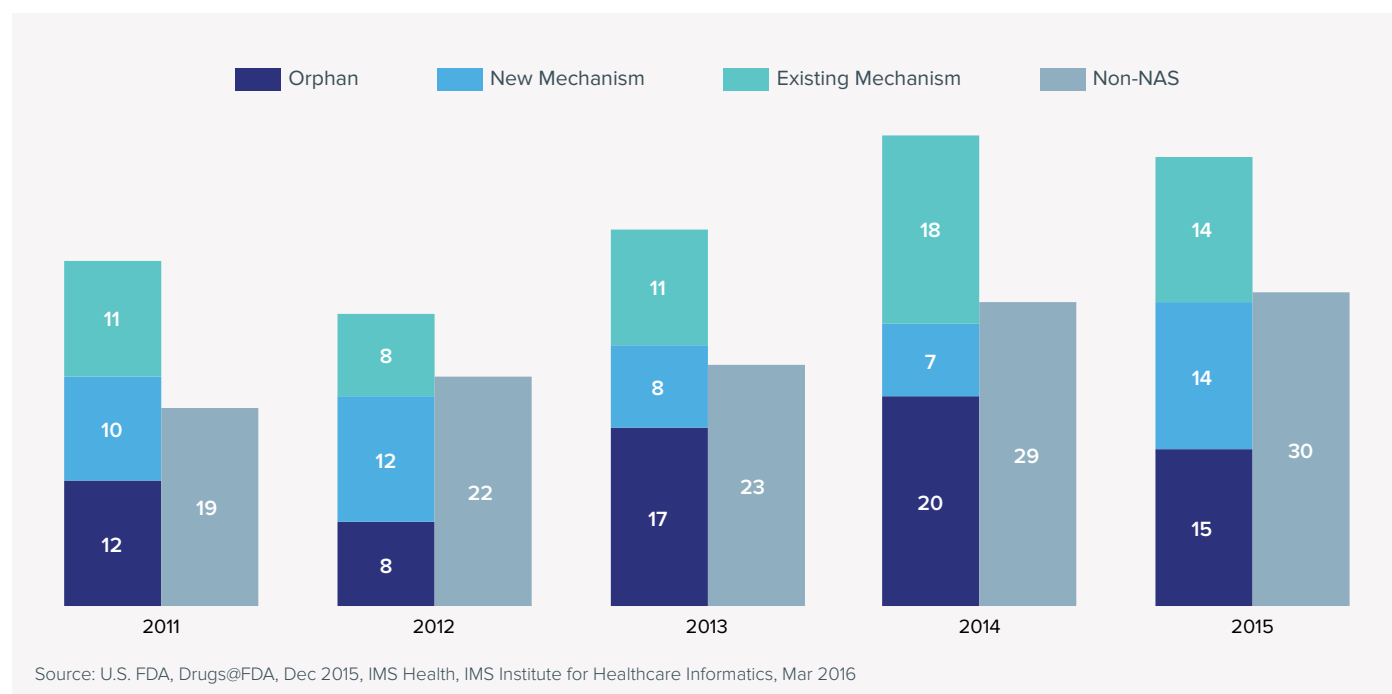
- Spending on diabetes medicines increased by \$1.6 billion or an estimated 8.2% on a net basis in 2015, compared with 30.1% growth on an invoice basis.
- Off-invoice discounts and rebates on existing and new brands – including patient cost savings programs – are estimated to offset \$8.6 billion of the invoice price growth in 2015.
- Nearly half of the \$10.1Bn invoice price growth was for insulins, however, all of the increase and more was offset by rebates and price concessions.
- Invoice spending on DPP-IV inhibitors increased \$1.4Bn or 21.6% to \$8.1Bn.
- Invoice spending on SGLT2s, the newest class of diabetes medicines, nearly tripled, rising \$2.0Bn to \$3.2Bn.
- GLP-1 agonists invoice spending rose \$1.2Bn to \$4.0Bn.
- The glitazones market shrunk from \$4.4Bn in 2011 to \$166Mn in 2015 due to safety concerns.

Chart notes:

Diabetes market includes prescription bound products and OTC insulins. Other diabetes category includes sulphonylureas, biguanides, glucosidase inhibitors, glinides, insulin devices, glucagon, and combination therapies. Invoice sales and growth values are based on IMS Health's audits of wholesaler transactions. Net sales and growth values denote company recognized revenue after discounts, rebates and other price concessions.

Launches of innovative medicines remained at high levels in 2015 with a total of 73 new brands emerging in 2015

Chart 13: New Active Substances (NAS) and Non-NASs Launched in the U.S. 2011–2015



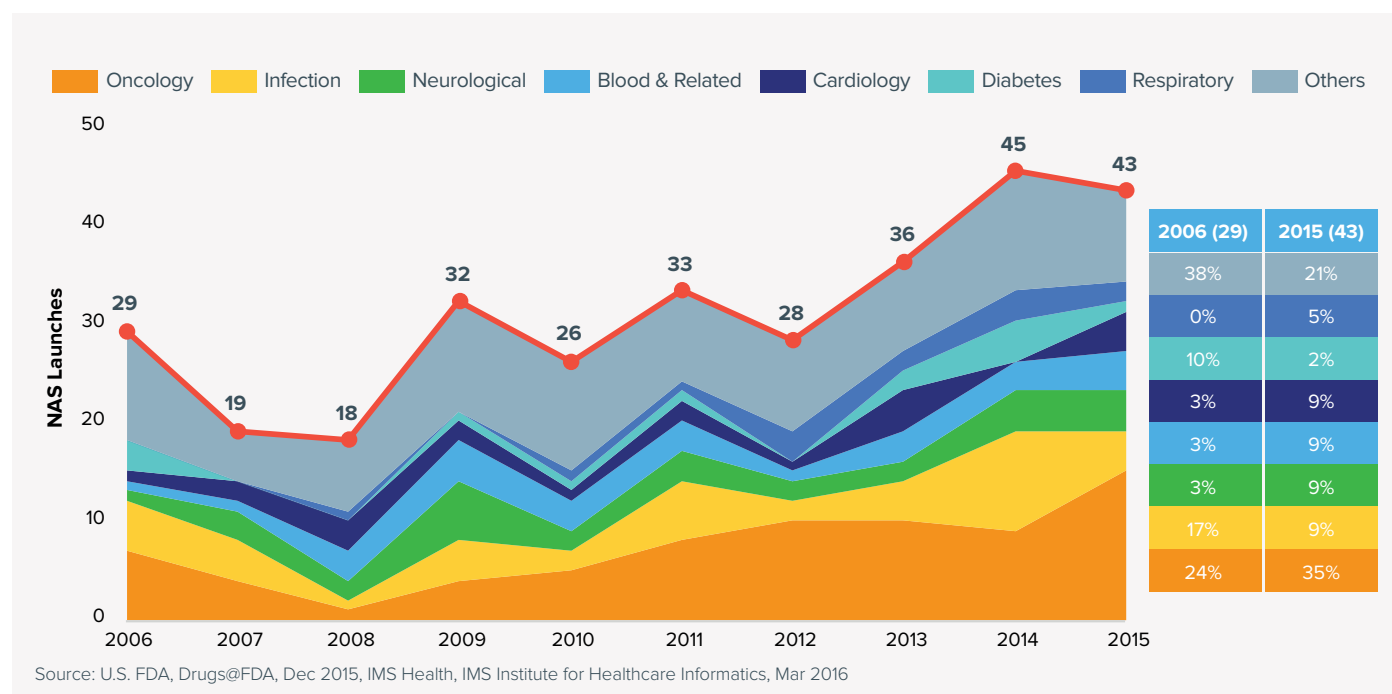
- Forty-three NASs were launched in 2015, a third with FDA orphan designation.
- In 2015, the number of non-orphan innovative drug launches doubled from the prior year, and is the most since tracking began in 2002.
- In the past five years, 72 orphan drugs were launched, including 15 in 2015, compared with 37 total from 2006 to 2010.
- Two-thirds of all orphan drugs were for oncology indications, while the remaining indications targeted rare diseases such as hemophilia B and cystic fibrosis.
- Innovative products included the first oncolytic virus therapy, new treatments for congestive heart failure in over a decade, the first in a new class of cholesterol-lowering medicines (PCSK9 inhibitors), and the first treatment for hypoactive sexual desire disorder for women.
- Among the 30 non-NAS new brand launches were treatments for pancreatic cancer, hepatitis C, and the first FDA approved biosimilar, along with new dosing and administration options to improve treatment adherence.

Chart notes:

A New Active Substance (NAS) is a new molecular entity, new biologic entity, or a new combination medicine in which at least one element is new. Annual NAS counts are determined by U.S. launch date, not FDA approval date. Non-NAS refers to new brands launched that are not classified as NASs (e.g. combination therapies, alternative dosing or treatment administration options). New Mechanism refers to the first product with a new mechanism of action for its FDA approved indication. Existing Mechanism refers to subsequent products with existing mechanisms of action for an indication. Orphans are medicines with one or more orphan indications approved by the FDA at product launch.

Oncology medicines comprise more than one-third of all launches in 2015

Chart 14: New Active Substances (NAS) by Therapy Area Launched in the U.S. 2006–2015



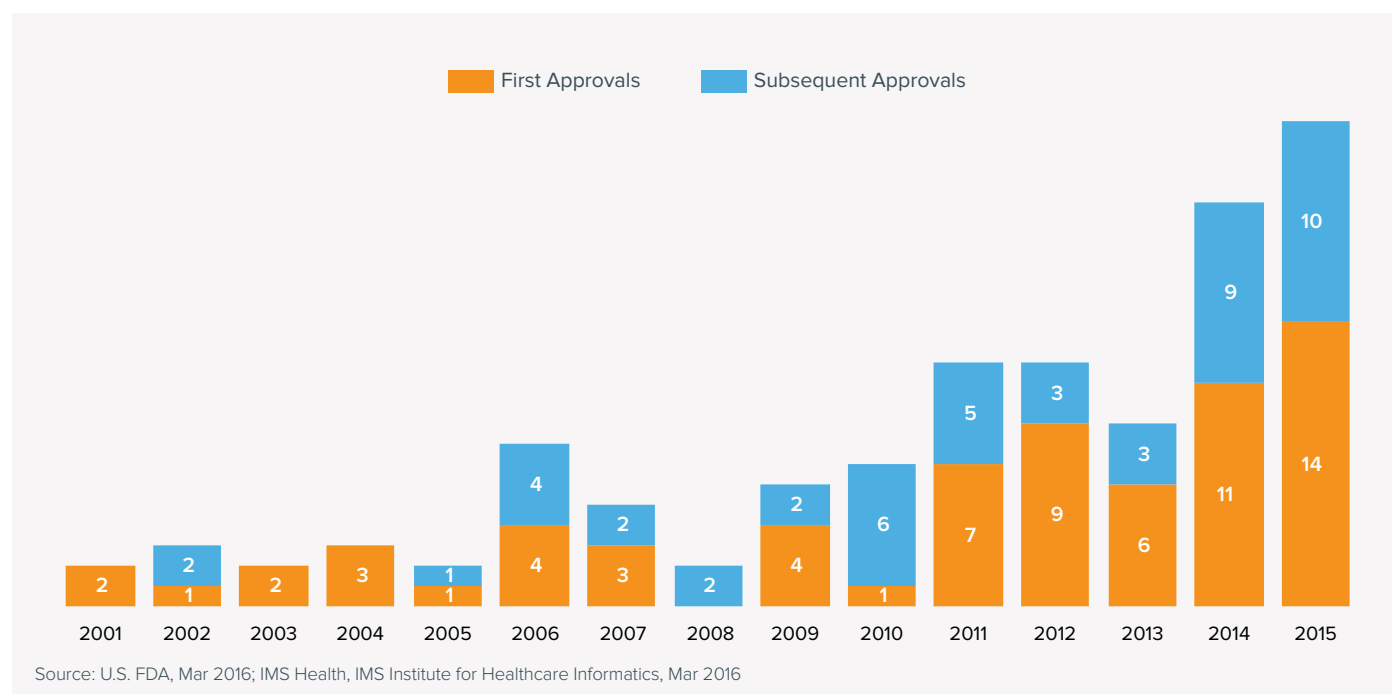
- The top three therapeutic areas, oncology, infection and neurological disorders, account for half of all NAS launches in five of the past 10 years.
- Oncology medicines launched in the past five years have primarily been targeted therapies, which target gene mutations in cancer cells, minimizing impact to surrounding healthy cells, and have been shown to work across a number of tumor types.
- The second largest number of launches in the past 10 years has been for infectious disease medicines including hepatitis C, HIV and bacterial infections, facilitated by the FDA Qualified Infectious Disease Program (QIDP).
- Neurological disorders, including epilepsy, multiple sclerosis and various mental health disorders make up the third most prevalent disease area for launches over the past 10 years.

Chart notes:

A New Active Substance (NAS) is a new molecular entity, new biologic entity, or a new combination medicine in which at least one element is new. Annual NAS counts are determined by U.S. launch date, not FDA approval date.

A growing number of additional indications are being approved for existing targeted oncology drugs

Chart 15: Targeted Oncology Medicine FDA Approval Type by Year



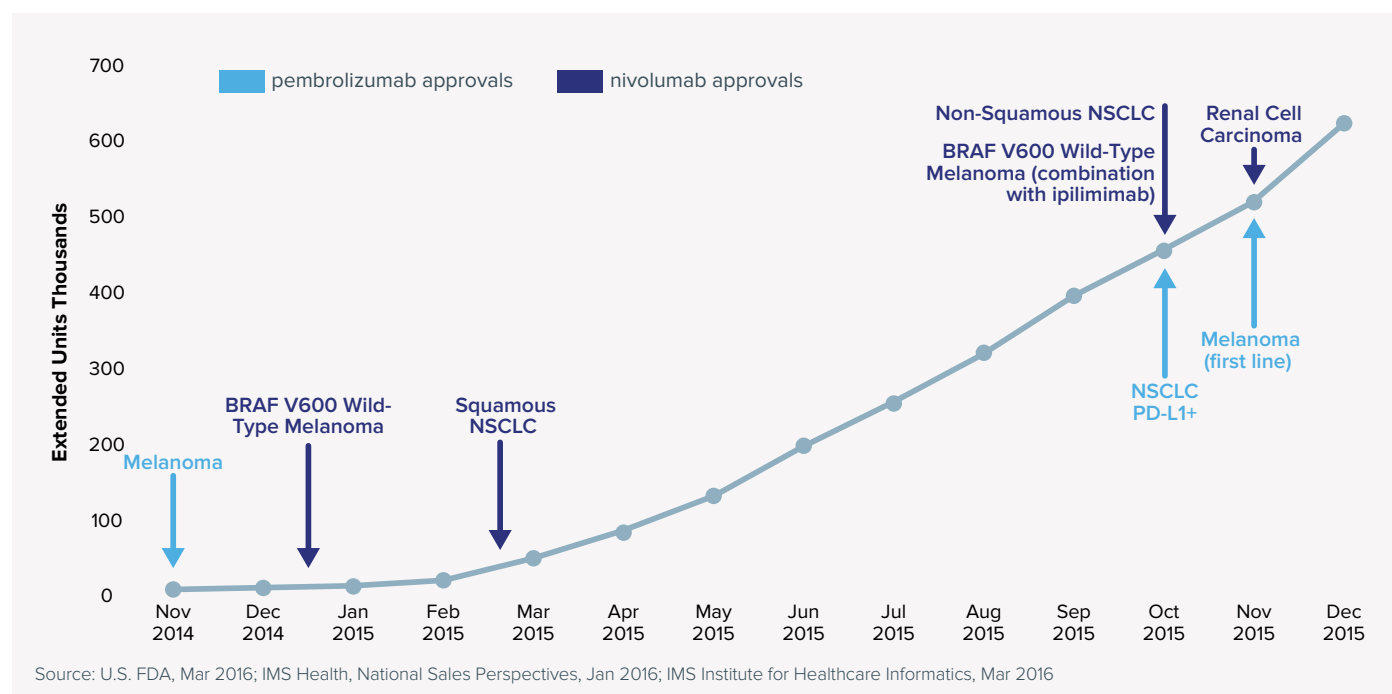
- The number of targeted oncology drug indications, both first approval and subsequent approvals, is higher in 2015 than at any time in the past.
- In 2015, 10 additional FDA approvals were granted, all of which were for medicines originally approved in the past five years.
- Targeted oncology medicines launched in the past five years (42) have garnered 17 additional FDA approvals.
- As treatments for cancer become more targeted, precise and less toxic, additional treatments options are being approved through smaller and faster clinical trials.
- Targeting immune checkpoints, PD-1 inhibitors are effective across a number of tumor types, including melanoma, hepatocellular carcinoma, glioblastoma, lung, kidney, breast, ovarian, pancreatic and esophageal cancers.

Chart notes:

Approvals are defined as FDA approved monotherapies or combination therapies, FDA-approved line extensions (e.g. from treatment after a prior therapy to preferred treatment), and subsequent FDA approved indications for treatment of disease sites not covered by the first FDA approval.

Rapid uptake of the new immuno-oncology drugs reflect their remarkable clinical profile and expansion of indications

Chart 16: Volume of Immuno-Oncology PD-1 Inhibitor Use



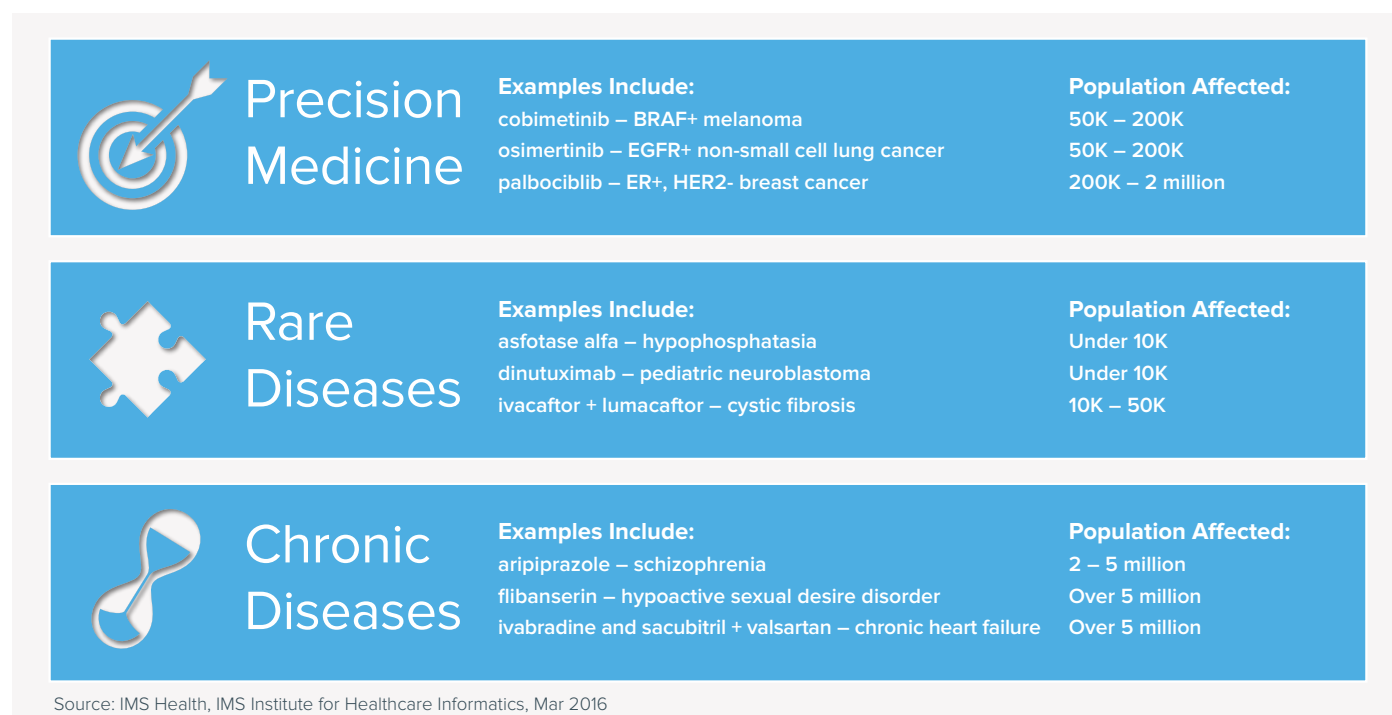
- The much anticipated immuno-oncology market was launched at the end of 2014 with two treatments for melanoma entering the oncology market.
- The success of the first PD-1 inhibitor, pembrolizumab, has been hampered by a narrow indication based on biomarker status, whereas use of nivolumab is not limited by biomarker status.
- Over 135 clinical trials for additional indications across 30 tumor types exist between the two currently approved PD-1 inhibitors.
- The promising PD-L1 inhibitor atezolizumab has Phase III trials in the pipeline for bladder cancer, breast cancer, non-small cell lung cancer and renal cell cancer.
- Other PD-1 and PD-L1 inhibitors in the pipeline include three indications for durvalumab (Ph III) with breakthrough status for PD-L1+ bladder cancer, and avelumab which has Phase III trials for four indications, including breakthrough status for the rare Merkel Cell carcinoma.

Chart notes:

PD-1 and PD-L1 refer to programmed death 1 (a receptor) and programmed death-ligand 1; BRAF is a gene that makes a protein called B-Raf; NSCLC refers to non-small cell lung cancer. All indications are for metastatic disease and second line or lower treatment sequence unless otherwise indicated. Months represent three month rolling average.

Notable NAS drug launches include precision medicines, rare disease treatments, and chronic disease medicines

Chart 17: NAS Launches



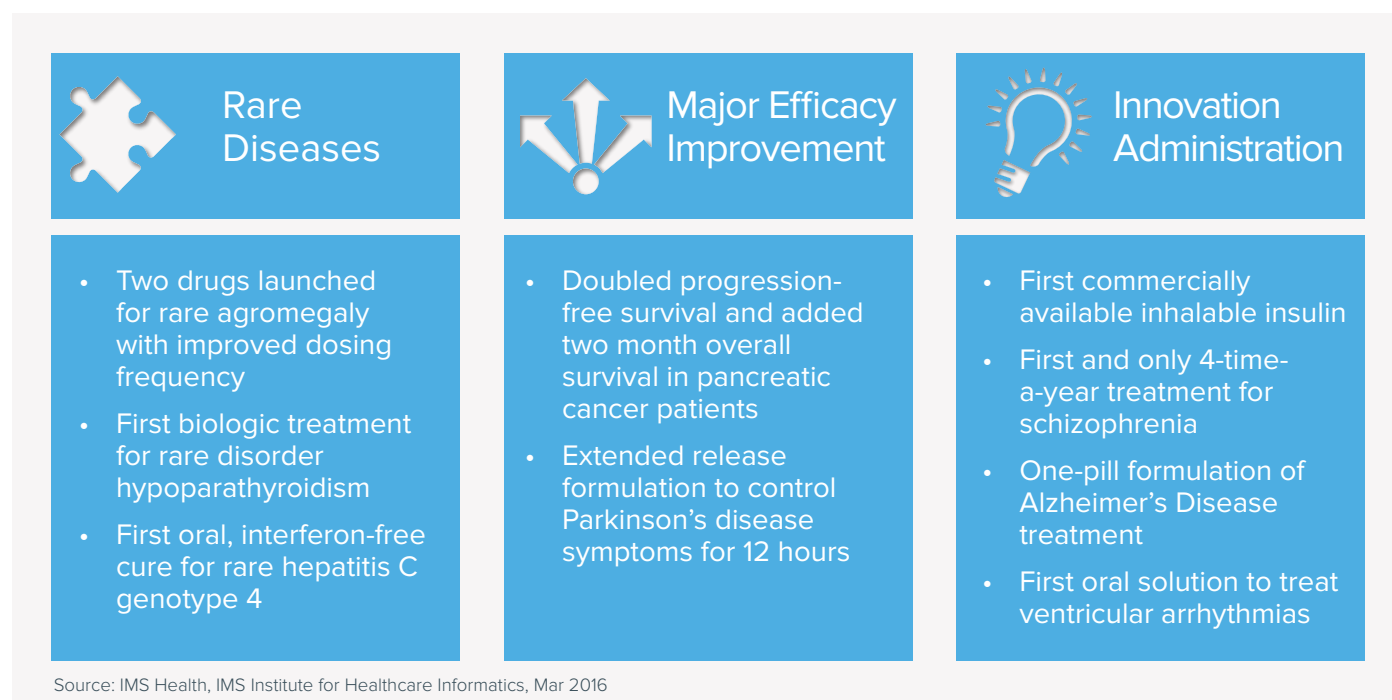
- FDA orphan-designated drugs launched in 2015 provide treatment options for almost 900,000 patients living with a rare disease.
- A drug for bile acid synthesis disorders received a Rare Pediatric Disease Review voucher, a program designed to encourage more research for unmet disease populations.
- Five of the seven FDA Breakthrough-designated drugs launched in 2015 were FDA orphan-designated treatments for cystic fibrosis, hypophosphatasia, lung cancer and multiple myeloma.
- Treatments targeting chronic diseases accounted for 50% of all NASs launched in 2015, 75% of which target patient populations in the millions of people affected by cardiac, metabolic and mental health conditions.
- Treatments for blood and heart conditions comprise more than a third of drugs launched for chronic diseases in 2015, targeting congestive heart failure, hypercholesterolemia, and complications such as stroke and blood clots in patients with atrial fibrillation.

Chart notes:

A New Active Substance (NAS) is a new molecular entity, new biologic entity, or a new combination medicine in which at least one element is new. Annual NAS counts are determined by U.S. launch date, not FDA approval date. Orphans are drugs with one or more orphan indications approved by the FDA at product launch.

Thirty new brands based on existing medicines were launched offering improvements that address patient adherence and unmet needs

Chart 18: Non-NAS Launches



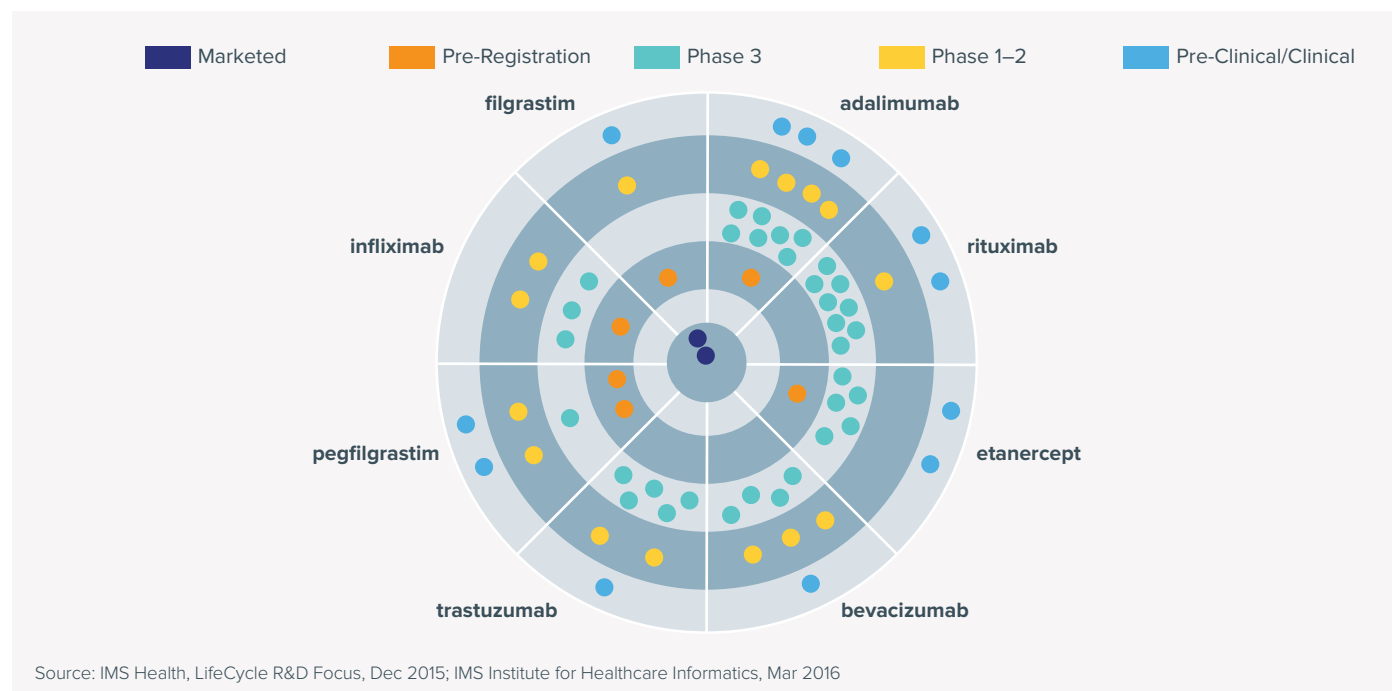
- An HPV 9-valent vaccine was launched in February 2015, providing protection against five more types of HPV and the potential to prevent up to 90% of cervical cancers.
- Five additional options were launched for diabetes patients, including the first inhalable insulin, two new combinations and two options providing easier insulin administration.
- Three new HIV products were launched providing patients with additional treatment options against drug resistance and reduced pill burden for combination regimens.
- Sufferers of chronic obstructive pulmonary disorder (COPD) received two new options for disease management, both options demonstrating greater efficacy and once-daily dosing schedule.

Chart notes:

Orphans are drugs with one or more orphan indications approved by the FDA at product launch. ALK+ NSCLC refers to non-small cell lung cancer patients with the anaplastic lymphoma kinase (ALK) gene mutation. HPV refers to Human Papilloma Virus.

Significant advances occurred in 2015 for biosimilars, including the first approval and a growing pipeline in development

Chart 19: U.S. Biosimilar Pipeline for Biologics with the Greatest Number of Biosimilar Candidates



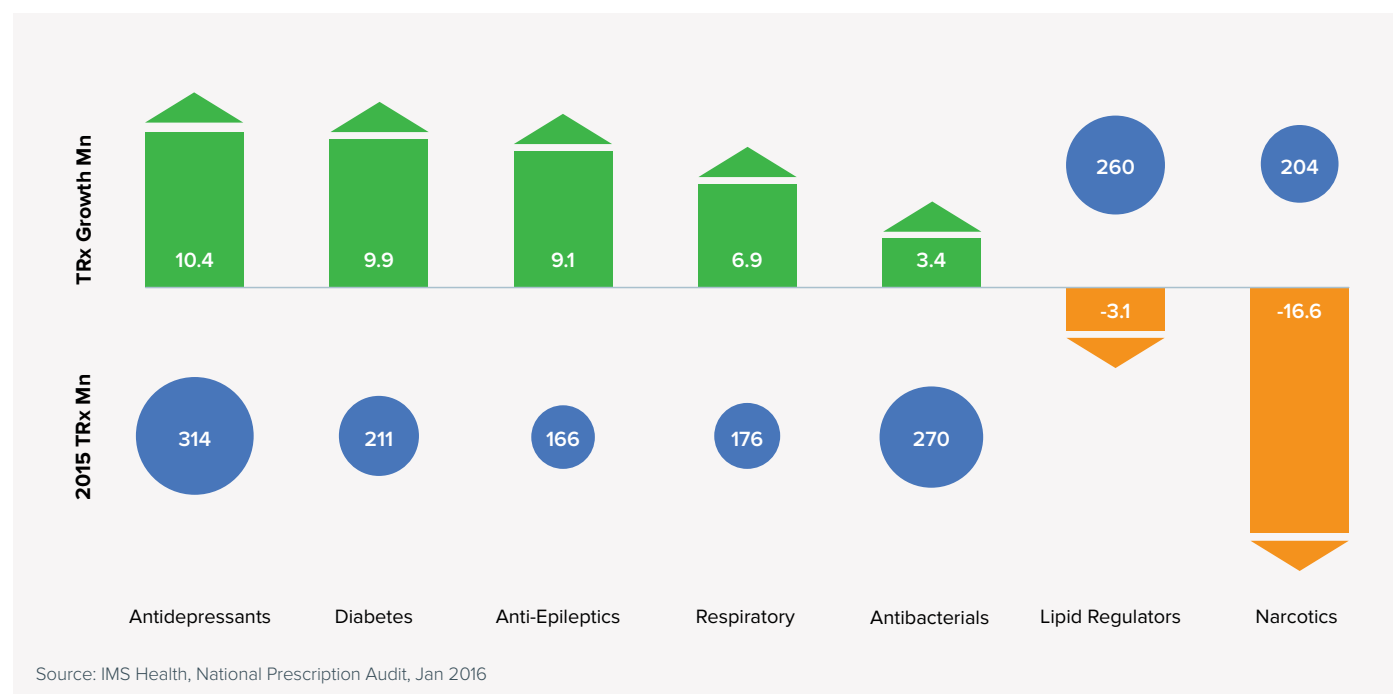
- In March 2015, the first biosimilar was approved via the biosimilar pathway (Zarxio – filgrastim) and launched in August 2015; the first non-original biologics, Granix and Omnitrope, were approved previously through alternative FDA pathways.
- As of December 2015, filgrastim biosimilars had contributed savings of over \$72 million, with Zarxio gaining 5% of sales after five months on the market.
- In 2015, 11 states passed legislation limiting the substitution of biologics to biosimilars deemed interchangeable by the FDA, bringing the total number of states with laws restricting substitution of biologics to 18.
- The price difference between the originator and first non-original biologic was 16% on an invoice price basis.
- Insulin glargine received final FDA approval as a “follow-on product” in December 2015 and is expected to launch in December of 2016.
- At the end of 2015, seven biosimilar applications were pending via the FDA biosimilar pathway, several with PDUFA dates in 2016.
- Lack of FDA guidance on interchangeability creates a different uptake environment than for the small molecule generic market, whereby biosimilars will need to compete with brands to be first choice by providers.

Chart notes:

Biosimilar pathway refers to the 2009 Biologics Price Competition and Innovation Act (BPCIA) 351(k) pathway. Omnitrope was approved in 2006 via the 505(b)(2) pathway and Granix was approved as an original biologic (BLA). States passing provision in 2015 include CA, CO, GA, IL, LA, NJ, NC, TN, TX, UT, and WA.

Total prescription demand increased by 1.0% in 2015 to 4.4Bn, with notable changes in select therapy areas

Chart 20: Select Therapy Areas Impacting Prescription Growth in 2015



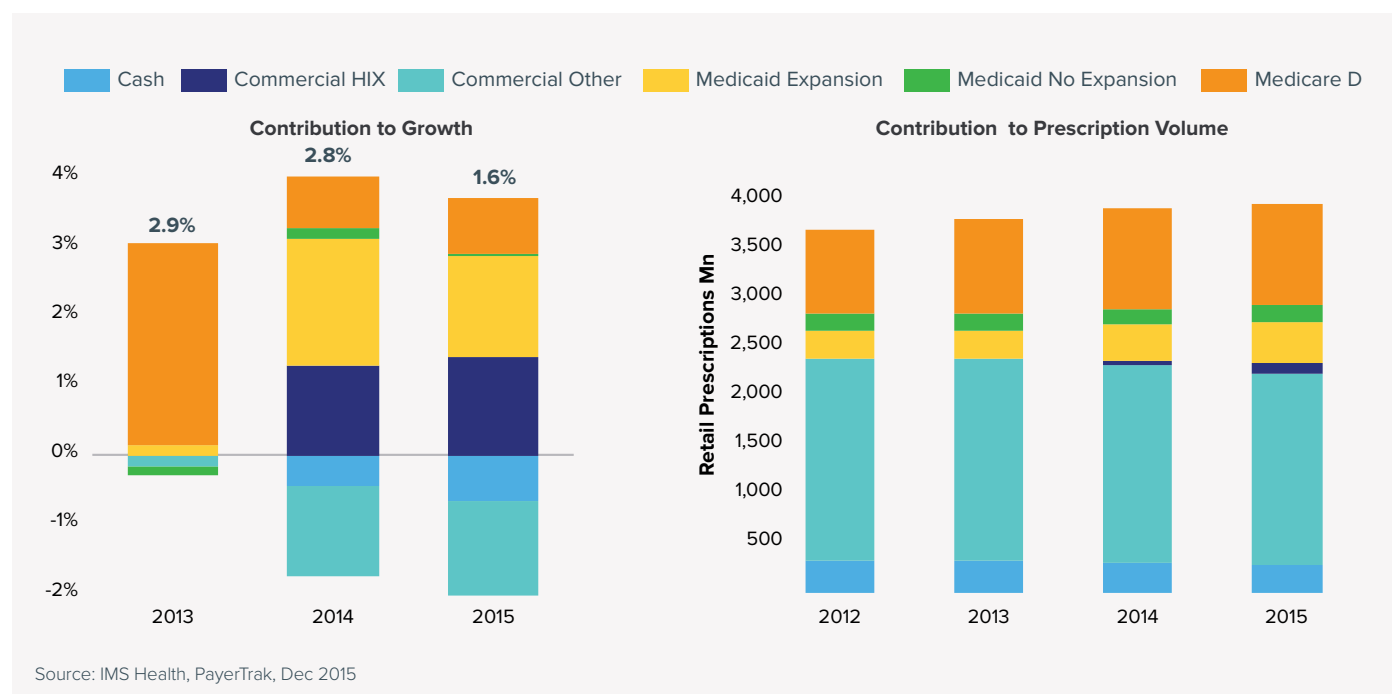
- Total prescription demand increased 1.0% in 2015 as 42.8Mn more prescriptions were dispensed in retail, mail, and long-term care pharmacies.
- Nationally, prescription demand increased 3.4% for antidepressants, 4.1% for respiratory, 4.9% for diabetes and 5.8% in anti-epileptics.
- Prescription volume shifted away from branded statins to generic atorvastatin, and overall demand for lipid regulators declined.
- Over 16 million fewer prescriptions were filled for narcotic analgesics, driven mainly by a sharp decrease in prescriptions for acetaminophen-hydrocodone, whereas prescriptions for oxycodone, another controlled substance, increased 5.3%.

Chart notes:

Therapy areas based on proprietary IMS Health definitions.

Affordable Care Act provisions have impacted the mix of payer types driving recent retail prescription growth

Chart 21: Retail Prescription Growth and Volume by Payer Type



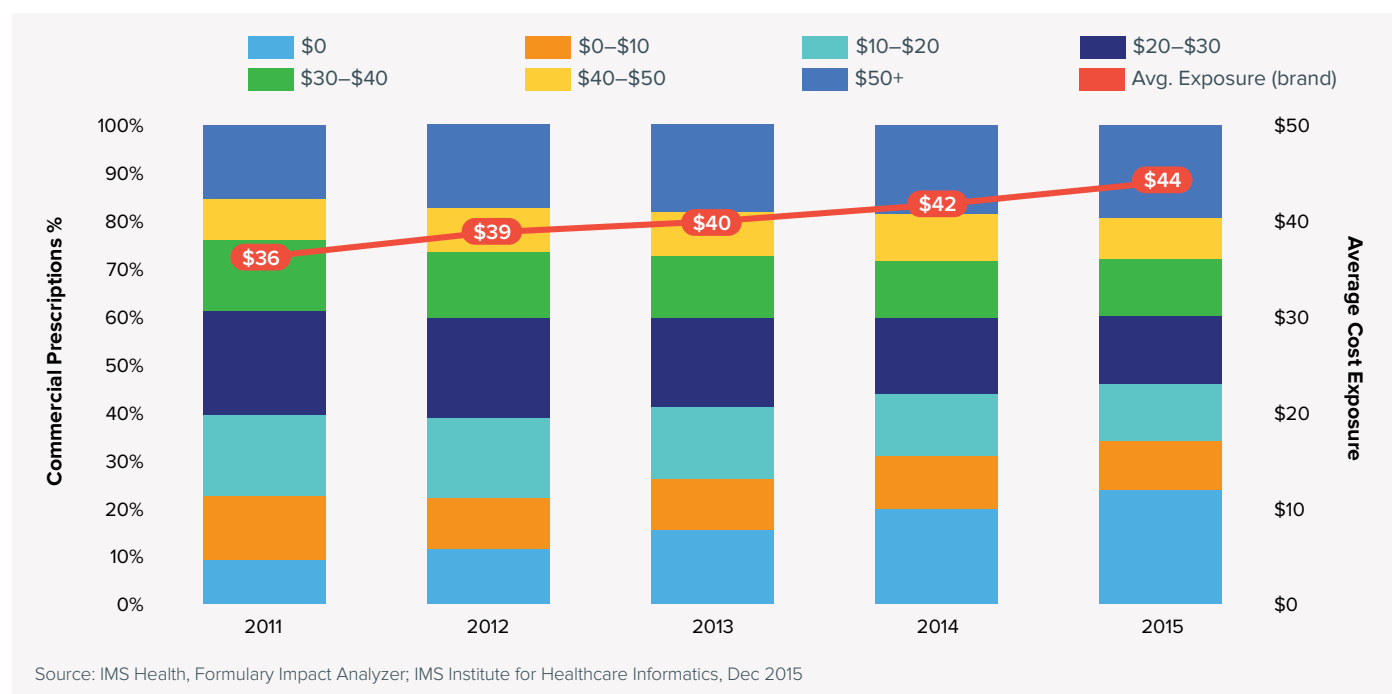
- Provisions of the Affordable Care Act (ACA) that provided coverage to the uninsured through Medicaid expansion and health exchange (HIX) plans have been the leading driver of prescription growth in the past two years.
- The increase in prescriptions filled by patients who enrolled in HIX plans has been offset by a decrease in scripts filled by patients with other commercial insurance.
- As more patients become insured, cash prescriptions continue to decline.
- Commercial (non-HIX) continues as the top payer type at 49% of all retail prescriptions but declined from 56% in 2012.
- Approximately 3% of retail prescriptions were filled by patients covered by exchange plans in 2015, up from 1% in 2014.
- The percent of retail prescriptions for Medicare continues to grow year over year.

Chart notes:

Retail only. Analysis includes 50 states and DC. Rolling quarter growth. Some exchange plans (HIX) may be categorized as other commercial plans. Medicaid expansion categorization based on the status of each state in 2015.

Patients faced higher average cost exposure for branded medicines as coinsurance and pharmacy deductible plans evolve

Chart 22: Patient Cost Exposure Distribution for Brands in Commercial Plans



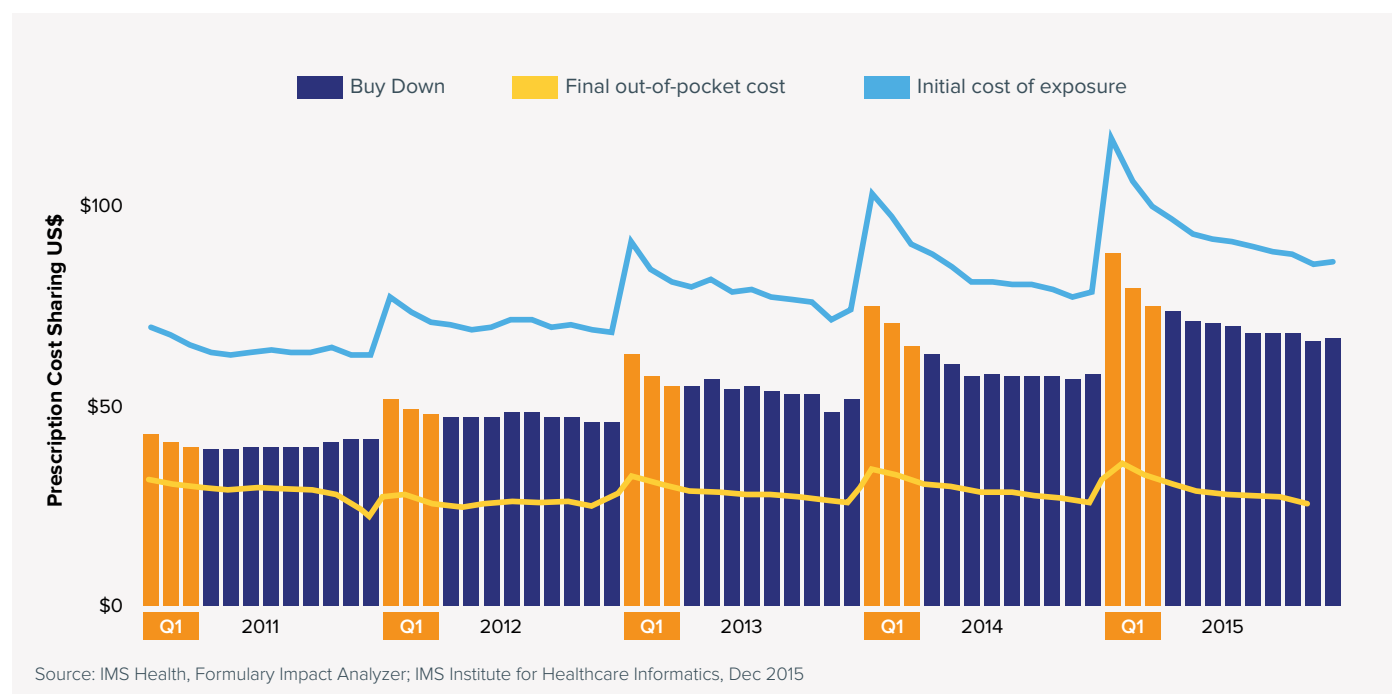
- The average patient cost exposure for brand prescriptions has increased by over 22% since 2011, rising from \$36 to \$44 per prescription.
- The proportion of brand prescriptions with patient cost exposure greater than \$50 increased to 17% in 2015 up from 14% in 2010.
- The proportion of brand prescriptions with \$0 patient cost exposure increased to 24% in 2015, up from 9% in 2011.
- Average generic patient cost exposure has remained at approximately \$8 since 2010.

Chart notes:

Cost exposure is calculated using paid and reversed claims where a coupon is the secondary payer and excludes instances in which a coupon is the primary payer, normalized to 30 days.

Brand manufacturer “buy-downs” have increased steadily to offset increasing patient cost exposure

Chart 23: Patient Cost-Sharing and Manufacturer Buy-Down (Commercial, Brands)



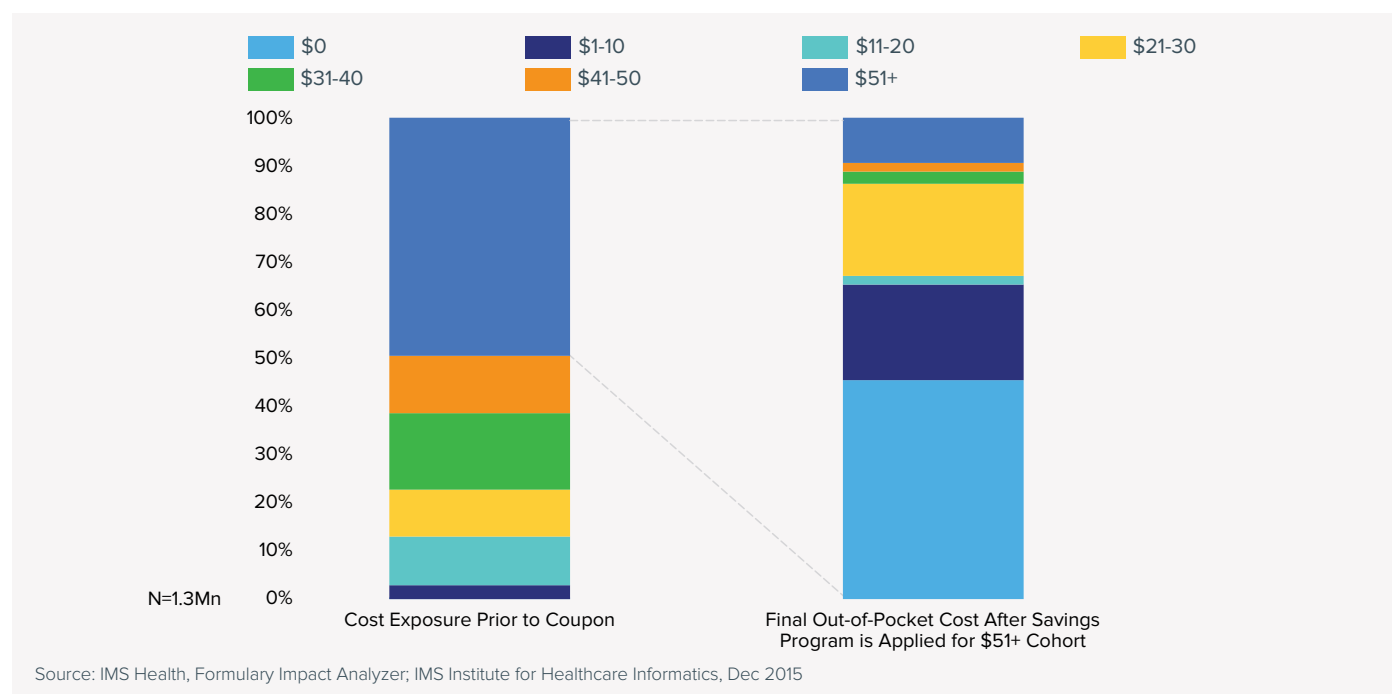
- As patient cost exposure has grown year over year, manufacturers have increased their “buy-downs”, through coupons and other patient savings programs offsetting cost such that final patient out-of-pocket remains fairly stable.
- Manufacturers’ buy-downs are especially high in the first quarter of a calendar year, when some patients are in the deductible phase of coverage.
- Manufacturer buy-downs, often in the form of coupons or vouchers, offload a significant amount of patient cost in certain therapy areas such as diabetes, respiratory, dermatology, autoimmune, and multiple sclerosis.

Chart notes:

Averages are calculated among paid claims where a co-pay card is used as the secondary payer and normalized to 30 days.

For diabetes patients, patient savings programs can significantly offset patient cost exposure, especially when that exceeds \$50

Chart 24: 2015 Patient Cost Exposure Distribution for Diabetes Prescriptions for Brands in Commercial Plans



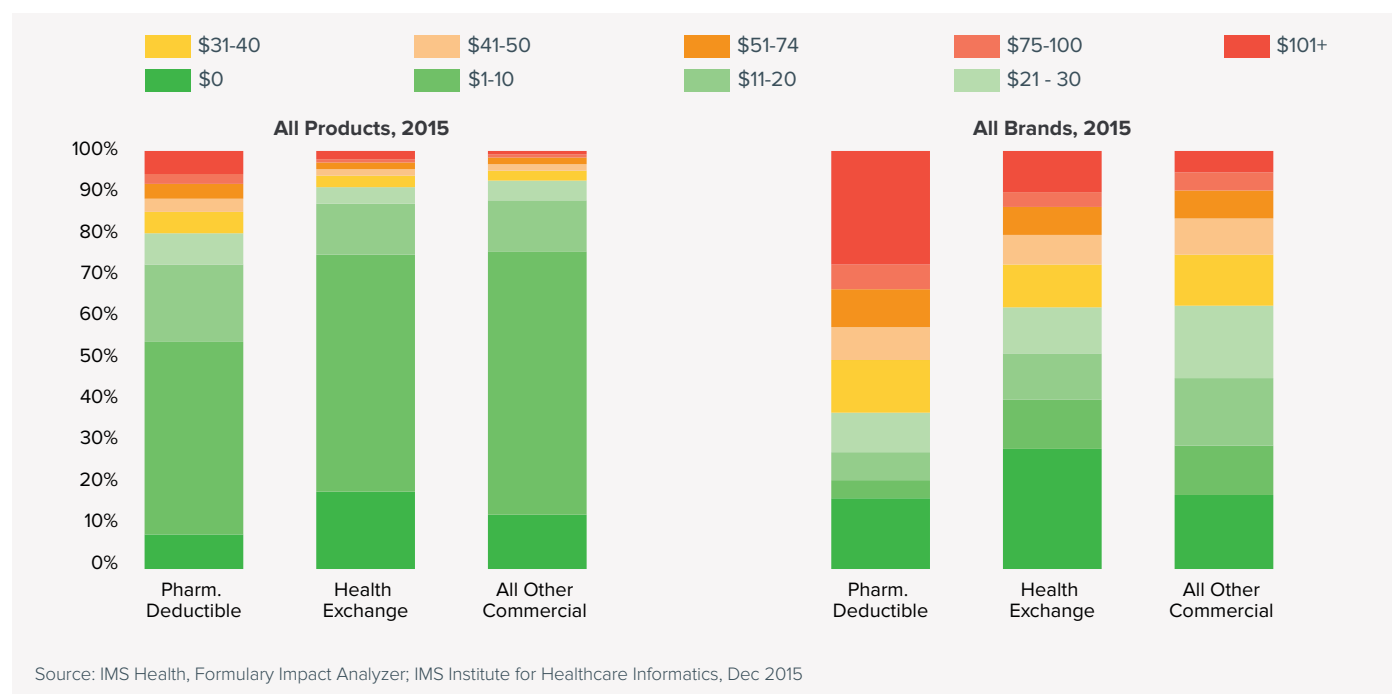
- Among diabetes claims with a patient savings program, such as coupons or vouchers, more than half of them are applied where patient cost exposure exceeds \$50.
- After application of a patient savings program, patients' final out-of-pocket costs vary across diabetes therapies, with most patients paying less than \$10.
- Patients and pharmacists must navigate the terms and conditions of patient savings programs to successfully benefit from the cost savings.
- While patient savings programs significantly reduce individual patient exposure, overall 4% of patients are still experiencing a \$50+ cost exposure in the diabetic market.
- The average buy down of patient cost exposure through patient savings programs varies by product with SGLT-2s driving the majority of the "buy-down" from the \$50 cohort in 2015.

Chart notes:

Cost exposure is calculated using paid and reversed claims where a coupon is the secondary payer and excludes instances in which a coupon is the primary payer, normalized to 30 days.

Even after patient savings programs are applied, patients with pharmacy deductibles have high cost exposure

Chart 25: Distribution of Commercial Prescriptions by Payer Type and Final Cost Sharing After Patient Savings Programs are Applied



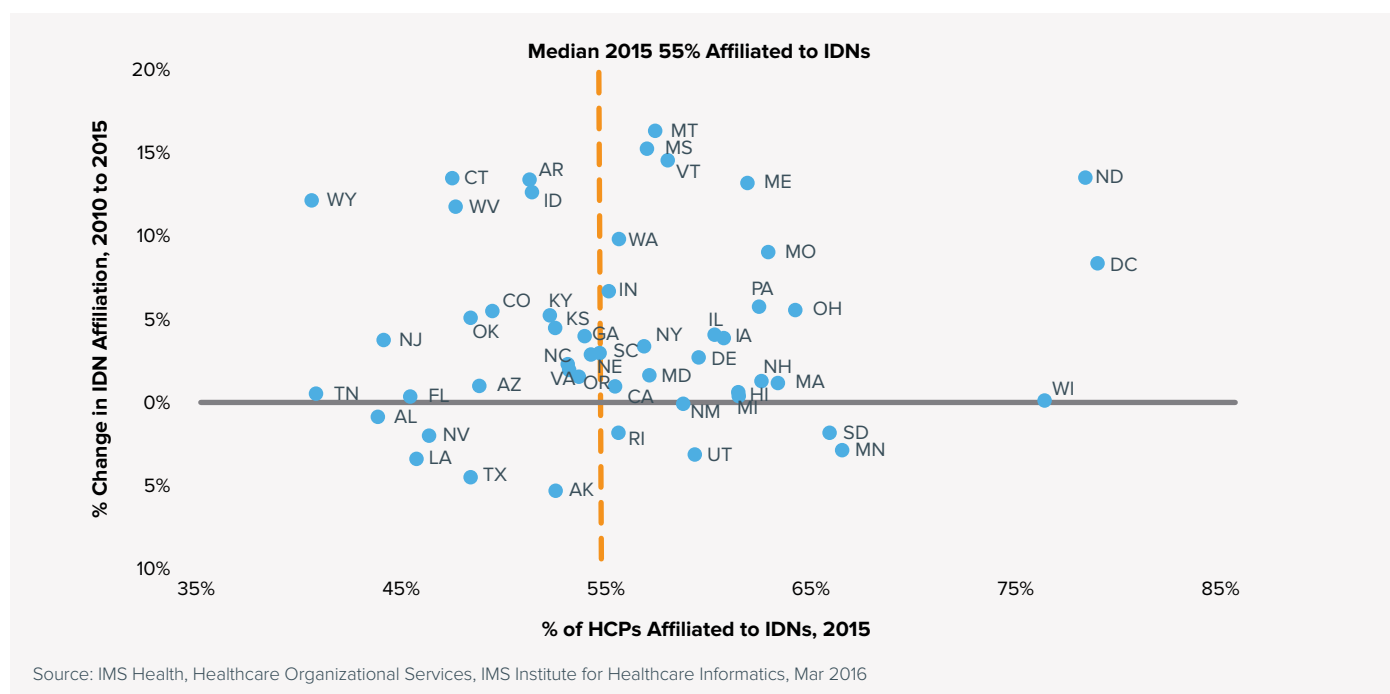
- Across all commercial pharmacy claims, deductible patients are still exposed to costs greater than \$50 in more than 10% of claims.
- Health Exchange and all other Commercial patients, have very similar cost exposures – more than 80% of which are exposed to costs of \$20 or less.
- Looking at brands only, approximately 40% of pharmacy deductible claims are exposed to costs greater than \$50.
- For brands, the proportion of costs greater than \$50 in Health Exchanges is approximately 20%, compared to 14% for all other commercial patients.
- Cost distributions by payer type vary by therapy area especially those with significant manufacturer buy-down such as in the diabetes market.

Chart notes:

Out-of-pocket costs include co-pay offsets through coupons; patient categories are defined using longitudinal data to identify deductible spending patterns or mode payer, normalized to 30 days.

Healthcare professional affiliations to Integrated Delivery Networks have continued to increase in most states

Chart 26: IDN Healthcare Professional (HCP) Affiliation and 5 year Change by State, 2010–2015



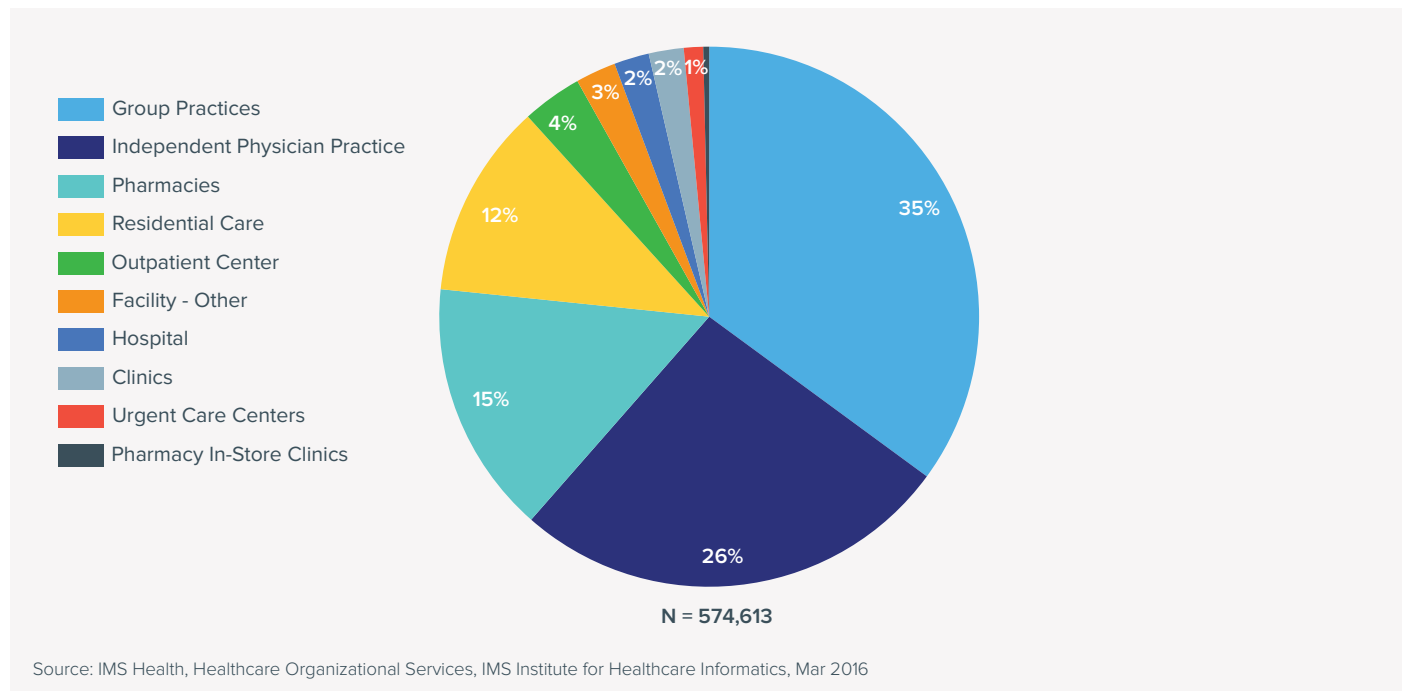
- From 2010 to 2015, 76% of states increased the level of Healthcare Professional (HCP) affiliation to Integrated Delivery Networks (IDNs).
- This growth supports IDN efforts to increase negotiating power with insurers, leverage economies of scale and drive pay for performance initiatives.
- Due to mergers and consolidations, 2015 represents the first time in 10 years that there was a decrease (1%) in the total number of IDNs nationally; however, this consolidation does not result in a contraction in the overall coverage or importance of IDNs.
- Over 54% of all healthcare providers (HCPs) nationally are affiliated with IDNs up from 51% in 2010.
- Ten states have experienced a growth in HCP IDN affiliations of 10% or greater in the past 5 years.
- As illustrated, there is significant variance in the percent of HCPs affiliated to IDNs by state and further variation exists by specialty type and at lower levels of geography.

Chart notes:

IDNs are defined as a healthcare system or network that includes an acute care hospital. For HCPs, the full universe of Healthcare Professional Services (HCPs) healthcare providers are included with the exception of Vets. Affiliation is determined by some type of contractual relationship with an IDN but does not infer an employment relationship. The percent of change metric is measured by HCP state IDN affiliations in Dec 2010 as compared to HCP state IDN affiliations in Dec 2015. HCPs that operate in more than one state are counted as affiliates in each state. Analysis based on 1.1Mn total unique HCPs for 2010 and 1.4Mn total unique HCPs for 2015.

Healthcare delivery centers addressing patient access and convenience are part of an increasingly diverse set of facilities

Chart 27: Healthcare Facility by Type for 2015



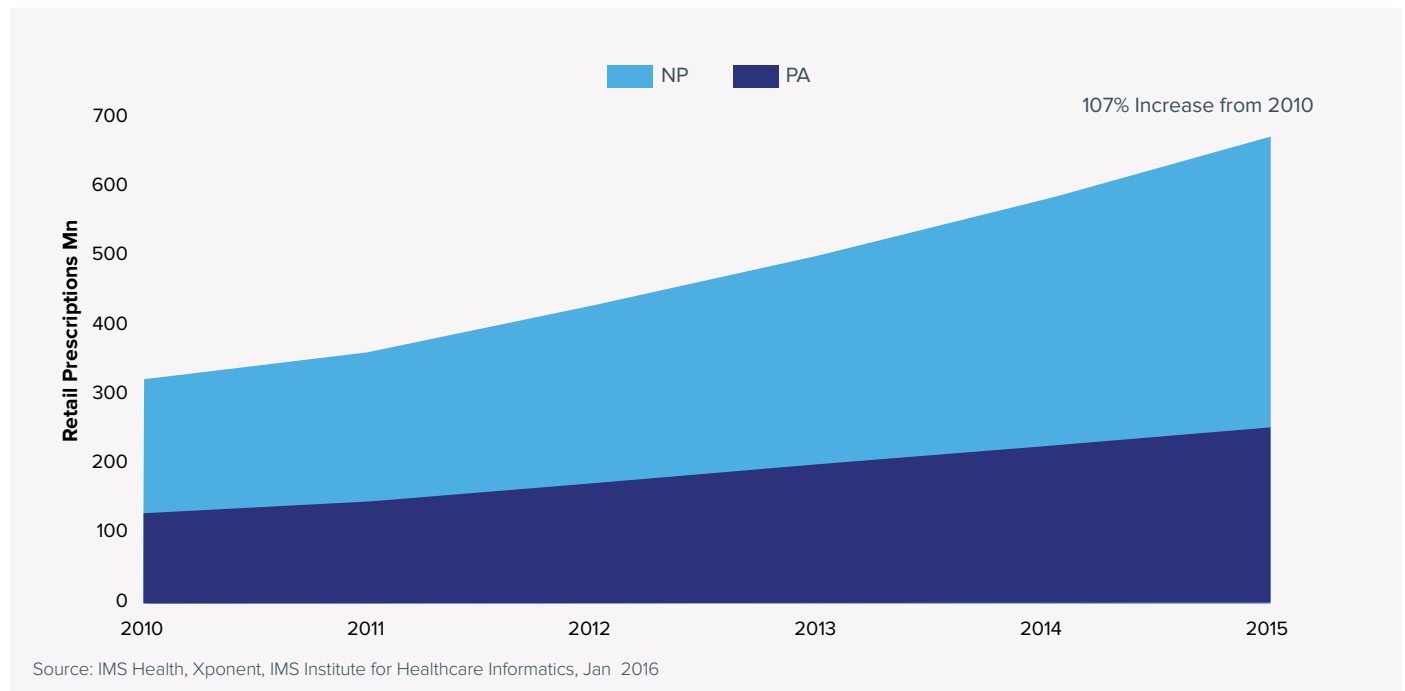
- The top-line number of healthcare facilities grew by 28% from 2010.
- Urgent Care Centers grew by 150% over the past 5 years, now making up 1% of all healthcare facilities.
- Pharmacy in-store clinics grew by 50% since 2010 but still only make up 0.4% of all facilities.
- While urgent care centers and pharmacy in-store-clinics only represent a small percentage of all facilities, their recent growth reflects the emergence of lower cost and more accessible treatment centers for non-emergency care.
- Seventy percent of urgent care centers are run independently without affiliation to a corporate owner or IDN.
- As of 2015, 82% of acute care hospitals are affiliated with an IDN, up 10% from 2010.
- As a percent of overall facilities, Arizona, West Virginia and North Carolina have the highest concentration of urgent care centers making up 2% of all facilities in those states.

Chart notes:

The cohort of Facility-Other includes facilities for alternative medicine, elder care, labs, correctional programs, and workplace wellness. All facilities from the Healthcare Organization services offering included except veterinarian facilities.

The number of prescriptions written by Nurse Practitioners and Physician Assistant's more than doubled over the past 5 years

Chart 28: Total Retail Prescriptions for NPs and PAs



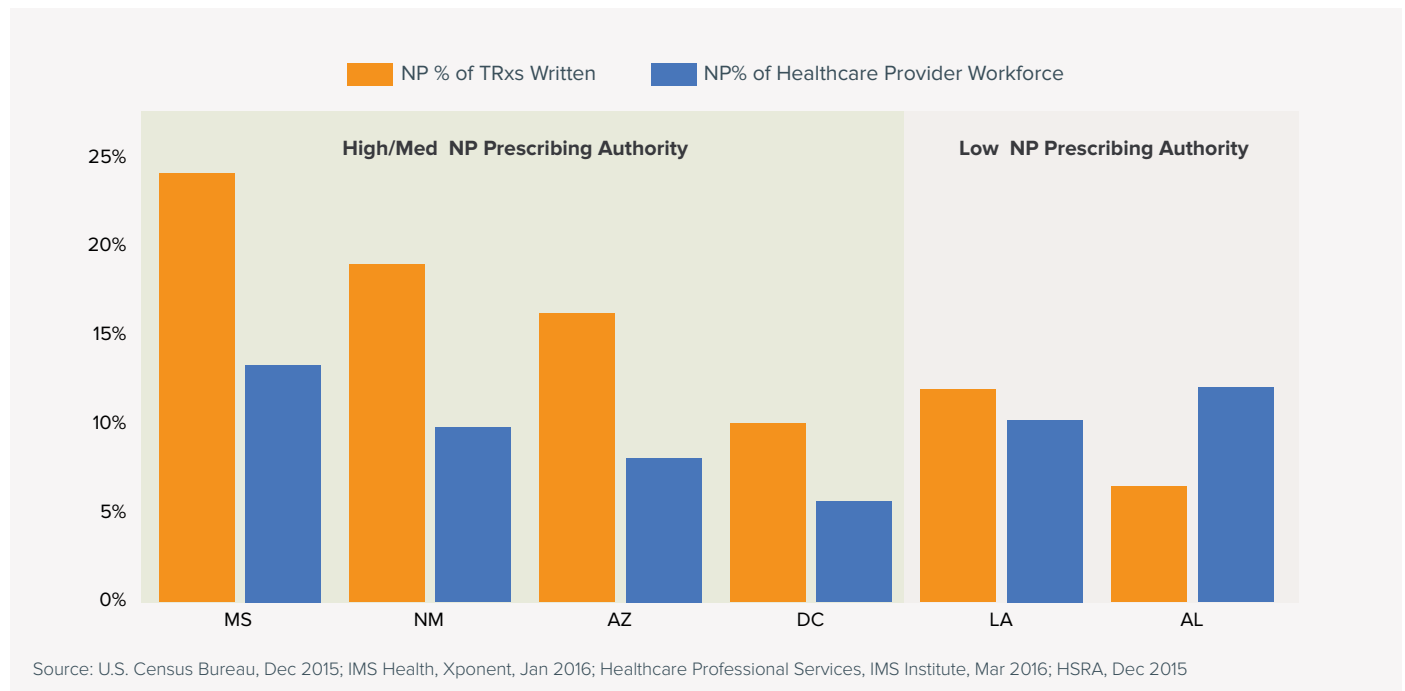
- As of 2015, 17% of all retail prescriptions were written by Nurse Practitioners (NPs) and Physician Assistants (PAs), up from 9% in 2010.
- Nationally, NP and PAs now make up 22% of the healthcare provider workforce.
- NPs and PAs combined wrote 676 million prescriptions in 2015 up from 327 million in 2010.
- The states of Wyoming and Idaho have the highest percentage (over 30%) of prescriptions written by NP/PAs.
- Alabama, Hawaii and Missouri have the lowest percent (under 8%) of prescriptions written by NP/PAs.
- The expansion of prescribing authority is determined by each state and not limited to NPs/PAs and has begun to expand, although limited, to other healthcare professional types such as psychologists, pharmacists and naturopaths.

Chart notes:

Includes all medicines across all markets for the retail channel.

Many states have expanded prescribing authority for NPs especially those with significant HCP shortage areas but some remain restricted

Chart 29: NP Prescribing and Workforce Details for Top HCP Shortage States



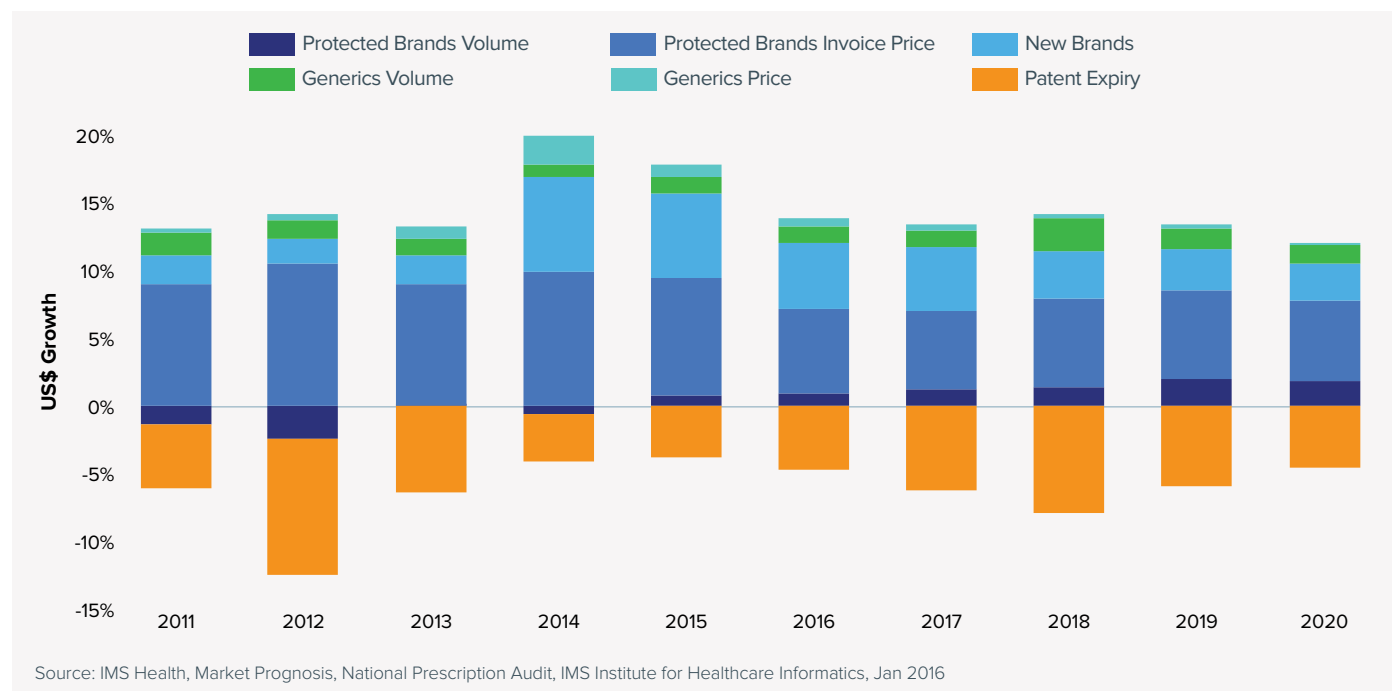
- Over 17% of states have fully expanded prescribing authority for NPs.
- As of 2015, 11% of all retail prescriptions were written by NPs, up from 6% in 2010.
- The prescriptive authority for NPs varies by state and may include restrictions on controlled substances.
- Based on the NP workforce availability and the lower percent of overall prescriptions written by NPs in AL and LA, it may be possible to further NPs in those states for addressing primary care coverage gaps.

Chart notes:

The top states with a healthcare provider gap are defined by the percent of population in healthcare professional s gap areas as compared to the overall state population. The six states shown have over 30% of their state's population in a healthcare professional shortage area as defined by an IMS Institute analysis using data from Health Resources and Services Administration (HSRA) division of the U.S. Department of Health and Human Services and the U.S. Census Bureau.

U.S. spending on medicines will reach \$610-640Bn in 2020 on an invoice price basis, with steady mid-single digit growth

Chart 30: U.S. Spending Growth 2010–2020 US\$Bn



- The U.S. will see a 46% increase in spending over the next five years, growing at a faster rate than the past five on an invoice price basis.
- The impact of patent expiries, while higher in absolute dollars in the next five years, will be lower in percentage contribution than the past five years.
- Price growth will continue at historic levels through 2020 after a period in 2013–15 where increases were much higher.
- Spending growth in 2014 and 2015 were atypical relative to the long-term trend driven by wider use of hepatitis C treatments, less patent expiry and higher price increases.
- Historically, protected brand volume has been a negative growth driver but in the next five years more protected brand spending will be driven by a new generation of brands gaining wider adoption.
- On a net price basis, U.S. spending is expected to reach \$370 to 400 billion in 2020, growing at 4–7%.
- The Affordable Care Act will continue to impact medicine spending over the next five years largely due to expanded insurance coverage, greater coordination of care and a shift to value based payment contracting.

Of the \$282Bn of growth to 2020 from brands, \$91Bn will result from new medicine launches in the next five years, the largest portion from oncology

Chart 31: Breakdown of Branded Product Elements of Growth

Element	Contribution to Spending Growth US\$Bn	Comment
Volume	\$36	Volumes of medicines remain largely unchanged on a per capita basis; mix of newer medicines contribute to higher average costs; small positive impact on volume including “mix” expected 2016–20, which had declining volume 2010–15
Price	\$155	Invoice price increases continue in the 10–12% range; subject to reduction from rebates and discounts
New	\$91	Robust flow of new medicines especially in oncology and with high value/price levels
Forecast Growth	\$282	Brand growth before adjusting for patent expiries and off-invoice discounts and rebates
Incremental Net Sales Adjustment (NSA)	-\$115	Estimated impact on branded medicine growth from increased rebates and discounts, reflecting payer consolidation, heightened competitiveness in many therapy classes and statutory price reduction mechanisms
Estimated Net Growth	\$167	

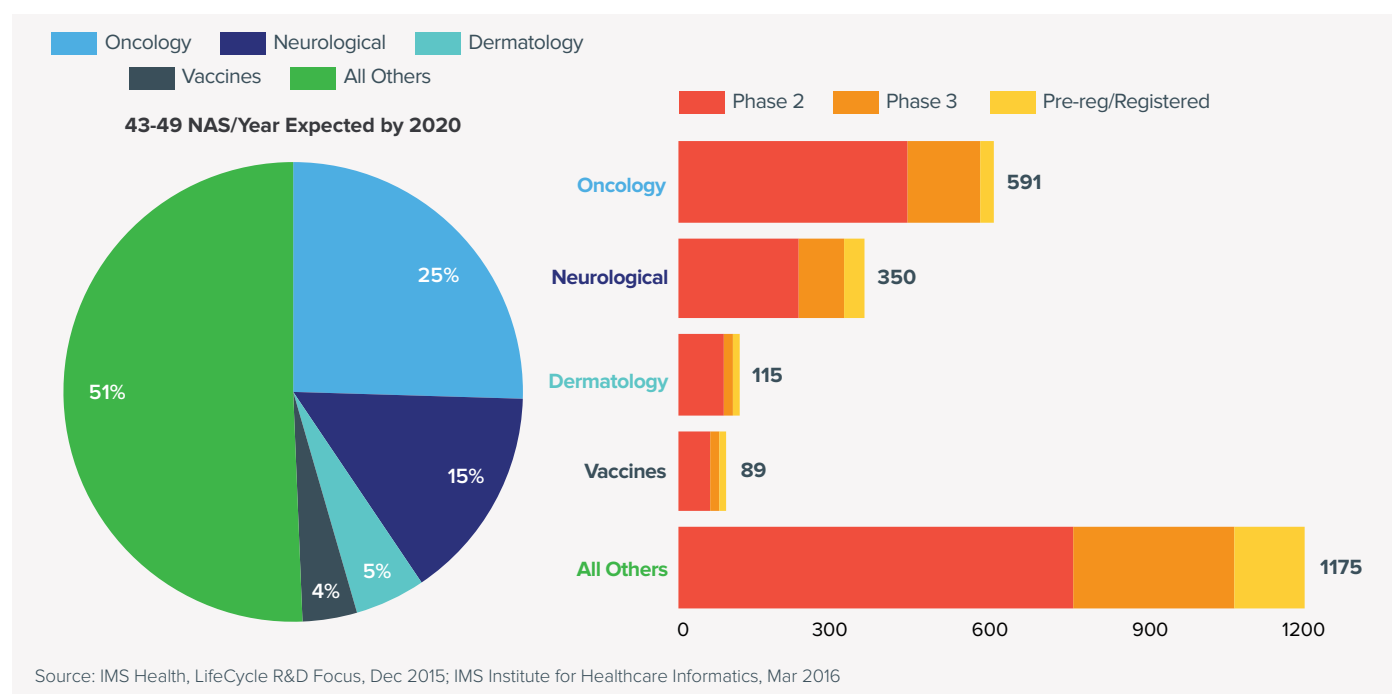
- Net brand spending growth is expected to be \$115Bn lower, or \$167Bn in total, reducing the absolute growth in the 5 year period by 41%.
- Of the \$167 billion of net brand growth prior to the impact of losses of exclusivity, \$65–70 billion is forecast to result from new medicines launched during that period.
- Existing branded medicines contribution to spending growth will be tied to increased usage of \$36Bn, and price increases, primarily in the U.S., largely offset by off-invoice discounts and rebates.
- Off-invoice discounts, rebates and other price concessions are expected to offset 74% of invoice price growth through 2020.

Chart notes:

Forecast growth reported on an invoice basis excluding off-invoice discounts and rebates. Forecast does not include the downside effects of patent expiries. Protected brand growth is split by volume and price. New brands segment includes products launched in the past twenty-four months. “Net” growth value based on expected company recognized revenue after discounts, rebates and other price concessions and resultant net prices.

The late phase R&D pipeline remains robust and will ensure an ongoing high number of new brand launches by 2020, especially cancer treatments

Chart 32: Late Phase R&D Pipeline by Top Therapy Areas



- The late phase pipeline includes 2,320 novel products, an increase of 9% from the 2014 pipeline analysis.
- Of the over 630 distinct research programs in Phase II or later research, 37% are for medicines in the specialty market.
- A quarter of the pipeline is comprised of oncology medicines, of which 25% are indicated for blood cancers.
- Pain, Alzheimer's disease and epilepsy are the top three indications in the neurological pipeline.
- Recently approved diagnostics for Alzheimer's disease improve clinical trial design efficiency and result in an uptick in the number of anti-Alzheimer's trials entering the pipeline.
- In the neurological market, three products are competing to be the first approved Duchenne muscular dystrophy treatment in the U.S., while the first orphan-designated cannabinoid product is in Phase III trials for pediatric epilepsy.

Chart notes:

Late phase pipeline is defined as active programs (activity in past 3 years) in Phase II through Registered. A New Active Substance (NAS) is a new molecular entity, new biologic entity, or a new combination medicine in which at least one element is new. CNS stands for central nervous system and includes the pain market. CTCL stands for cutaneous T-cell lymphoma. NSCLC stands for non-small cell lung cancer.

Notes on Sources

IMS National Sales Perspectives (NSP)[™] measures spending within the U.S. pharmaceutical market by pharmacies, clinics, hospitals and other healthcare providers. NSP reports 100% coverage of the retail and non-retail channels for national pharmaceutical sales at actual transaction prices. The prices do not reflect off-invoice price concessions that reduce the net amount received by manufacturers.

IMS National Prescription Audit (NPA)[™] is a suite of services that provides the industry standard source of national prescription activity for all products and markets.

IMS Xponent[®] is a suite of services that provides near census level coverage of dispensed prescription information at a prescriber and insurance plan level.

IMS NPA Market Dynamics[™] is a suite of services that leverages longitudinal tracking of anonymous patient data to analyze the treatment decisions and patterns at a prescriber level.

IMS PayerTrak[™] provides retail prescriptions by insurance plan and segments those plans into types of insurance including Medicare Part D, Medicaid (including Fee for Service and Managed Medicaid plans), Commercial Third Party insurance, and Cash (prescriptions without insurance).

IMS Healthcare Organization Services (HCOS)[™] is an organizational and affiliation reference for hospitals, long-term care and alternate care sites, medical group practices, outpatient surgery centers, diagnostic imaging centers, and home health agencies and the doctors associated with them. Organization data can be aligned and integrated with IMS professional, prescription and/or medicine spending data. The approximately 640,000 facilities includes single ownership relationships and multiple purchasing, distribution, academic and alliance relationships.

IMS Healthcare Professional Services (HCPS)[™] provides a comprehensive view of over 7.8 million professionals including key information such as professional profiles, profession, specialty and subspecialty, authorizations including SLN and DEA, license type and privilege, sample eligibility flag and industry identifiers such as ME and NPI numbers. Professional addresses utilize IMS Health's proprietary Address Intelligence, an algorithm that weighs address factors to determine a professional's current, previous, and best address.

IMS Formulary Impact Analyzer (FIA) provides insight into what impact popular utilization-control measures enforced by managed care organizations have had on prescription volumes including the dynamics that affect patient behavior in filling and/or refilling prescriptions. Formulary measures include tiered co-pay benefit designs, prior authorization restrictions, and often result in non-preferred prescriptions being rejected or switched at the pharmacy. FIA offers visibility to claims rejected for other reasons such as contraindications as well as those attempted to be refilled too soon. FIA sources include national and regional chains, independent pharmacies and a switch house providing a comprehensive view of retailers and across geographies.

IMS Market Prognosis is a comprehensive, strategic market forecasting publication that provides insight to decision makers about the economic and political issues that can affect spending on healthcare globally. It uses econometric modeling from the Economist Intelligence Unit to deliver in-depth analysis at a global, regional and country level about therapy class dynamics, distribution channel changes and brand vs. generic product spending.

IMS LifeCycle™ New Product Focus™ is a comprehensive worldwide tracking service of historical product launches since 1982. It includes information about product launches in each country, including the indication and price at the time of the initial launch, and covers more than 300, 000 launches.

IMS LifeCycle™ R&D Focus™ is a global database for evaluating the market for medicines, covering more than 31,000 drugs in R&D and over 8,900 drugs in active development worldwide. It includes information about the commercial, scientific and clinical features of the products, analyst predictions of future performance, and reference information on their regulatory stage globally.

Appendix

Top Therapeutic Classes by Prescriptions						
Dispensed Prescriptions Mn		2011	2012	2013	2014	2015
Total U.S. Market		4,014	4,155	4,236	4,325	4,368
1	Antihypertensives	649	691	701	705	706
2	Mental Health	495	511	523	537	547
3	Pain	472	484	481	483	470
4	Antibacterials	274	272	269	267	270
5	Lipid Regulators	255	266	264	263	260
6	Antidiabetes	174	186	193	201	211
7	Nervous System Disorders	148	157	168	179	188
8	Respiratory	153	157	162	169	176
9	Anti-Ulcerants	150	159	166	170	173
10	Thyroid Therapies	113	122	127	131	133
11	Dermatologicals	102	103	105	109	109
12	Hormonal Contraceptives	90	91	95	97	96
13	ADHD	73	76	80	83	87
14	Anticoagulants	73	76	77	78	78
15	Corticosteroids	55	60	62	65	68
16	GI Products	55	57	58	61	63
17	Nasal Preps Topical	46	48	51	56	52
18	Other Cardiovasculars	51	51	50	49	48
19	Ophthalmology	42	43	44	44	46
20	Benign Prostate Hyperplasia	34	36	37	40	41

Source: IMS Health, National Prescription Audit, Dec 2015

Appendix notes:

Therapy areas are based on proprietary IMS Health definitions. Includes prescription-bound products including insulins dispensed through chain and independent pharmacies, food store pharmacies, mail service pharmacies, and long-term care facilities. Excludes OTC products. IMS Health routinely updates its national audits, which may result in changes to previously reported market size and growth rates. Prescriptions are not adjusted for length of therapy; 90-day and 30-day prescriptions are both counted as one prescription.

Top Therapeutic Classes by Non-Discounted Spending						
Non-Discounted Spending US\$Bn		2011	2012	2013	2014	2015
Total U.S. Market		328.3	317.8	331.5	378.6	424.8
1	Diabetes	21.0	22.3	25.6	33.7	43.9
2	Oncology	24.1	25.6	28.1	33.1	39.1
3	Autoimmune	13.1	15.2	18.3	23.5	30.2
4	Respiratory	21.4	21.1	19.9	21.4	23.8
5	Mental Health	31.8	24.4	23.3	22.8	21.2
6	Pain	17.9	17.9	18.9	21.0	20.4
7	Viral Hepatitis	2.1	2.9	1.9	12.2	18.8
8	Multiple Sclerosis	7.8	9.1	11.9	15.0	17.7
9	HIV Antivirals	10.1	11.1	12.2	14.0	16.2
10	Lipid Regulators	21.7	16.6	13.5	13.5	13.3
11	Nervous System Disorders	6.9	7.0	8.2	9.6	11.2
12	ADHD	9.4	10.5	10.3	10.5	11.2
13	Dermatologicals	6.8	7.6	8.8	9.4	10.6
14	Antihypertensives	14.1	13.3	12.6	12.0	10.3
15	Anticoagulants	13.6	9.3	7.2	8.5	9.9
16	Vaccines excl flu	5.6	6.0	6.1	6.9	8.5
17	Antibacterials	9.5	7.8	8.8	8.6	8.1
18	Anti-Ulcerants	10.1	9.5	9.8	9.1	7.9
19	Other Cardiovasculars	4.2	4.6	5.2	6.4	7.4
20	GI Products	3.9	4.1	4.8	5.7	7.0

Source: IMS Health, National Sales Perspectives, Jan 2016

Appendix notes:

Therapy areas are based on proprietary IMS Health definitions. Includes prescription and insulin products sold into chain and independent pharmacies, food store pharmacies, mail service pharmacies, long-term care facilities, hospitals, clinics, and other institutional settings. Excludes OTC. IMS Health routinely updates its national audits, which may result in changes to previously reported market size and growth rates.

Top Medicines by Prescriptions						
Dispensed Prescriptions Mn		2011	2012	2013	2014	2015
Total U.S. Market		4,014	4,155	4,236	4,325	4,368
1	levothyroxine	105	112	117	120	121
2	lisinopril	89	99	102	104	106
3	acetaminophen/hydrocodone	137	136	129	119	97
4	atorvastatin	43	55	68	81	93
5	metoprolol	76	83	84	85	86
6	amlodipine	63	69	75	78	82
7	metformin	59	68	73	77	80
8	omeprazole	59	67	72	75	77
9	albuterol	57	61	64	67	70
10	simvastatin	97	89	80	73	66
11	gabapentin	33	39	44	51	57
12	amoxicillin	54	53	54	54	56
13	fluticasone	38	42	45	51	49
14	hydrochlorothiazide	48	51	50	49	49
15	alprazolam	49	49	50	49	49
16	azithromycin	56	55	49	47	48
17	furosemide	42	44	46	47	46
18	sertraline	38	40	42	44	46
19	losartan	19	28	34	39	44
20	tramadol	34	39	42	44	43

Source: IMS Health, National Prescription Audit, Dec 2015

Appendix notes:

Includes prescriptions and insulins dispensed through chain and independent pharmacies, food store pharmacies, mail service pharmacies, and long-term care facilities. Excludes OTC. IMS Health routinely updates its national audits, which may result in changes to previously reported market size and growth rates. Prescriptions are not adjusted for length of therapy; 90-day and 30-day prescriptions are both counted as one prescription. Table shows leading active-ingredients or fixed combinations of ingredients and includes both branded and generic products.

Top Medicines by Non-Discounted Spending						
Non-Discounted Spending US\$Bn		2011	2012	2013	2014	2015
Total U.S. Market		328.3	317.8	331.5	378.6	424.8
1	Harvoni	0.0	0.0	0.0	1.6	14.3
2	Humira	3.8	4.5	5.7	7.8	10.6
3	Enbrel	3.8	4.2	4.9	5.9	6.6
4	Crestor	4.5	4.8	5.3	5.7	6.3
5	Lantus SoloStar	1.7	2.3	3.3	4.8	5.8
6	Remicade	3.5	3.8	4.1	4.5	5.0
7	Advair Diskus	4.6	4.6	5.0	4.7	4.7
8	Abilify	5.0	5.4	6.3	7.6	4.4
9	Copaxone	3.2	3.5	3.8	4.0	4.4
10	Januvia	2.2	2.6	2.9	3.5	4.2
11	Neulasta	3.3	3.4	3.6	3.8	4.1
12	Lyrica	1.8	1.9	2.4	3.1	3.8
13	Lantus	2.1	2.2	2.6	3.5	3.8
14	Rituxan	3.0	3.1	3.3	3.5	3.6
15	Nexium	6.1	5.7	6.0	5.8	3.5
16	Tecfidera	0.0	0.0	1.0	2.9	3.5
17	Spiriva HandiHaler	2.4	2.7	3.0	3.3	3.4
18	Avastin	2.7	2.6	2.7	2.9	3.1
19	Sovaldi	0.0	0.0	0.1	7.8	3.0
20	Atripla	2.5	2.7	2.8	2.9	2.9

Source: IMS Health, National Sales Perspectives, Jan 2016

Appendix notes:

Includes prescription and insulin products sold into chain and independent pharmacies, food store pharmacies, mail service pharmacies, long-term care facilities, hospitals, clinics, and other institutional settings. Excludes OTC. IMS Health routinely updates its national audits, which may result in changes to previously reported market size and growth rates.

Dispensing Locations by Non-Discounted Spending					
Non-Discounted Spending US\$Bn	2011	2012	2013	2014	2015
Total U.S. Market	328.3	317.8	331.5	378.6	424.8
Retail And Mail	235.9	227.4	237.6	272.7	305.9
Chain Stores	109.8	106.3	109.8	121.8	130.7
Mail Service	63.9	60.9	65.3	82.3	97.4
Independent	38.3	36.5	36.7	42.2	48.0
Food Stores	23.8	23.6	25.7	26.4	29.7
Non-Retail	92.4	90.4	93.9	105.9	118.9
Clinics	38.6	39.5	42.3	48.4	56.2
Non-Federal Hospital	28.1	28.1	28.4	30.2	33.4
Long-Term Care	15.2	13.9	14.0	16.2	16.7
HMO	2.6	2.8	3.0	3.9	4.9
Home Health Care	2.7	2.7	2.8	3.4	3.9
Federal Facilities	4.2	2.5	2.4	2.7	2.7
Miscellaneous	1.0	0.9	0.9	1.0	1.1

Source: IMS Health, National Sales Perspectives, Jan 2016

Appendix notes:

Includes prescription-bound products including insulin products and excluding other products such as OTC. IMS Health routinely updates its national audits, which may result in changes to previously reported market size and growth rates.

Dispensed Prescriptions by Dispensing Locations Unadjusted for Prescription Length					
Dispensed Prescriptions Mn	2011	2012	2013	2014	2015
Total U.S. Market	4,014	4,155	4,236	4,325	4,368
Retail and Mail	3,686	3,825	3,871	3,941	3,990
Chain stores	2,206	2,303	2,386	2,475	2,522
Independent	739	738	736	738	739
Food stores	481	521	516	516	522
Mail service	260	262	233	212	207
Non-Retail	329	330	366	384	378
Long-term care	329	330	366	384	378

Source: IMS Health, National Prescription Audit, Dec 2015

Dispensed Prescriptions by Dispensing Locations Adjusted for Prescription Length					
Adjusted Dispensed Prescriptions Mn	2011	2012	2013	2014	2015
Total U.S. Market	4,988	5,265	5,382	5,506	5,603
Retail and Mail	4,654	4,931	5,012	5,117	5,220
Chain stores	2,547	2,753	2,903	3,053	3,151
Independent	825	833	843	855	865
Food stores	573	630	632	636	649
Mail service	709	715	634	573	555
Non-Retail	333	335	370	389	383
Long-term care	333	335	370	389	383

Source: IMS Health, National Prescription Audit; IMS Institute for Healthcare Informatics, Dec 2015

Appendix notes:

Includes prescriptions and insulins dispensed through chain and independent pharmacies, food store pharmacies, mail service pharmacies, and long-term care facilities. IMS Health routinely updates its national audits, which may result in changes to previously reported market size and growth rates. Prescriptions for 90 days have been used to estimate 30 day prescriptions in all dispensing locations. 90-day prescriptions represented 10.9% of retail rising to 11.64% in 2015.

Dispensing by Payment Type for Retail Prescriptions					
Dispensed Prescriptions Mn	2011	2012	2013	2014	2015
Retail Prescriptions	3,426	3,562	3,638	3,729	3,783
Commercial Third-Party	58.4%	55.9%	54.2%	52.7%	51.9%
Medicare Part D	21.5%	23.2%	25.4%	25.9%	26.3%
Medicaid	12.8%	12.2%	11.9%	13.5%	14.8%
Cash	7.3%	8.7%	8.5%	7.8%	7.1%

Source: IMS Health, National Prescription Audit; PayerTrak, Dec 2015

Appendix notes:

Report reflects prescription-bound products including insulins and excluding other products such as OTC.

PayerTrak provides payer-type segmentation for retail prescriptions only.

Medicaid includes both Fee for Service and Managed Medicaid.

Non-Discounted Spending and Dispensing by Product Type					
Spending US\$Bn	2011	2012	2013	2014	2015
Total U.S. Market	328.3	317.8	331.5	378.6	424.8
Brands	74.5%	71.7%	71.0%	72.1%	73.3%
Unbranded Generics	13.6%	16.1%	16.9%	16.9%	16.0%
Branded Generics	11.9%	12.2%	12.1%	11.0%	10.7%
Dispensed prescriptions Mn	2011	2012	2013	2014	2015
Total U.S. Market	4,014	4,155	4,236	4,325	4,368
Brands	20.2%	15.9%	13.6%	12.3%	11.3%
Unbranded Generics	72.7%	77.7%	80.5%	82.1%	83.4%
Branded Generics	7.1%	6.4%	5.9%	5.6%	5.3%

Source: IMS Health, National Sales Perspective, National Prescription Audit, Jan 2016

Appendix notes:

Includes prescriptions and insulins dispensed by chain and independent pharmacies, food store pharmacies, mail service pharmacies, and long-term care facilities. Spending figures also include sales into hospitals, clinics, and other institutional settings. IMS Health routinely updates its national audits, which may result in changes to previously reported market size and growth rates.

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About the Institute

The IMS Institute for Healthcare Informatics leverages collaborative relationships in the public and private sectors to strengthen the vital role of information in advancing healthcare globally. Its mission is to provide key policy setters and decision makers in the global health sector with unique and transformational insights into healthcare dynamics derived from granular analysis of information.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved patient care. With access to IMS Health's extensive global data assets and analytics, the Institute works in tandem with a broad set of healthcare stakeholders, including government agencies, academic institutions, the life sciences industry and payers, to drive a research agenda dedicated to addressing today's healthcare challenges.

By collaborating on research of common interest, it builds on a long-standing and extensive tradition of using IMS Health information and expertise to support the advancement of evidence-based healthcare around the world.

Research Agenda

The research agenda for the Institute centers on five areas considered vital to the advancement of healthcare globally:

- The effective use of information by healthcare stakeholders globally to improve health outcomes, reduce costs and increase access to available treatments.
- Optimizing the performance of medical care through better understanding of disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.
- Understanding the future global role for biopharmaceuticals, the dynamics that shape the market and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of innovation in health system products, processes and delivery systems, and the business and policy systems that drive innovation.
- Informing and advancing the healthcare agendas in developing nations through information and analysis.

Guiding Principles

The Institute operates from a set of Guiding Principles:

- The advancement of healthcare globally is a vital, continuous process.
- Timely, high-quality and relevant information is critical to sound healthcare decision making.
- Insights gained from information and analysis should be made widely available to healthcare stakeholders.
- Effective use of information is often complex, requiring unique knowledge and expertise.
- The ongoing innovation and reform in all aspects of healthcare require a dynamic approach to understanding the entire healthcare system.
- Personal health information is confidential and patient privacy must be protected.
- The private sector has a valuable role to play in collaborating with the public sector related to the use of healthcare data.

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