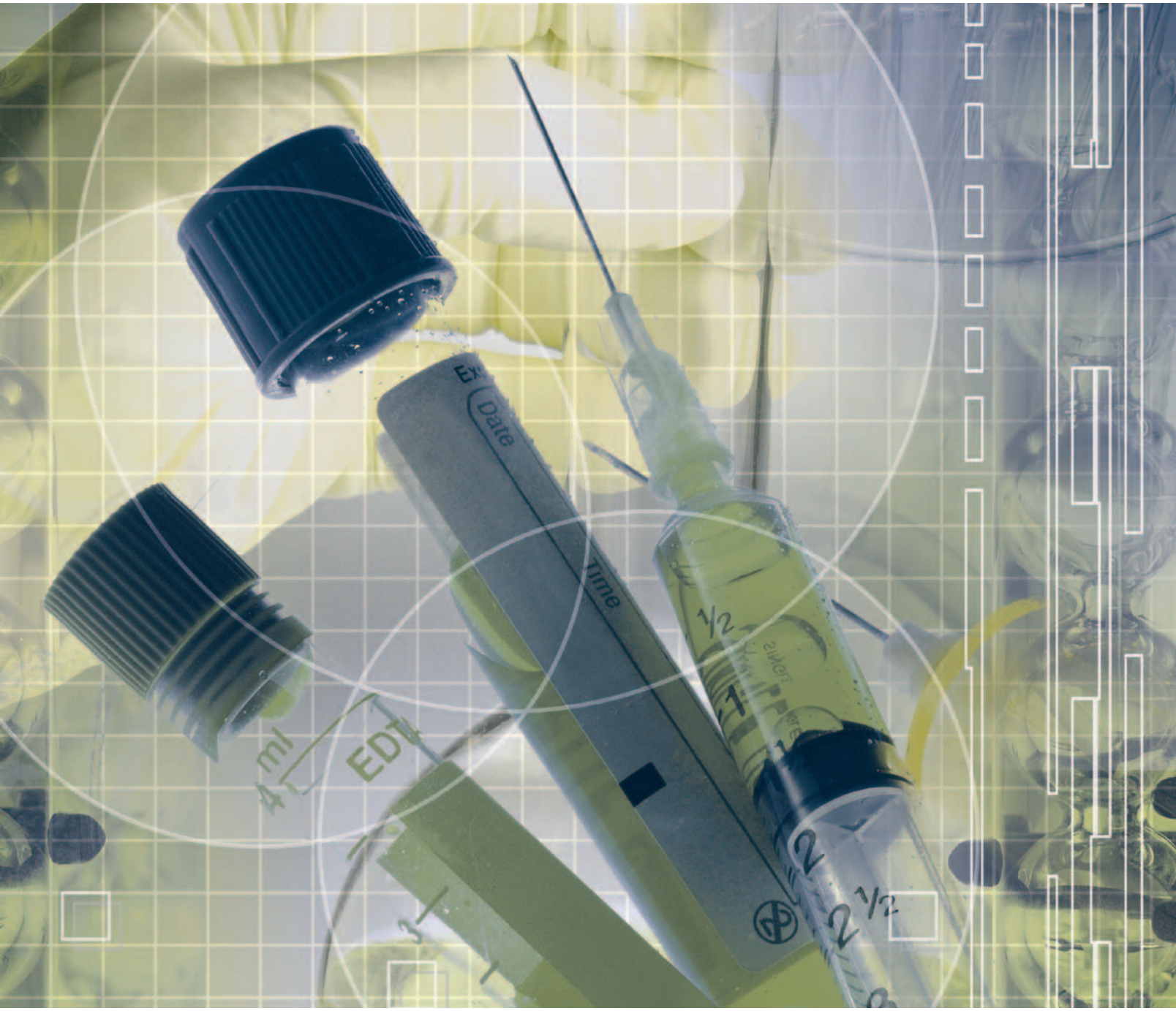
MEDICAL INJECTABLES & ONCOLOGY TREND REPORT™

2010 FIRST EDITION



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Injectable Drugs: Giving You the Data You Need

It is my pleasure to present you with the 2010 ICORE Healthcare Medical Injectables & Oncology Trend Report™. It is the first of what will be an annual publication. The purpose of our investment in this report is straightforward: Back in 2003 when ICORE Healthcare first began assisting payors in managing medical injectables, no reference or benchmark data existed. Frankly, this has continued to be the case until the release of this report, since few, if any, benefit managers are able to review and assess medical benefit injectable claims.

Assessing medical injectable use, costs, and trends is more critical now than ever, since five of the top 16 drugs in 2009 (based upon sales dollars) were specialty drugs, whereas it is expected that 11 drugs of the top 16 will be injectable or specialty products by 2012 (see table below). While trend reports regarding specialty and oral chemotherapy products paid under the pharmacy benefit exist today, no source exists for injectables paid under a payor's medical benefit, where top drugs such as Neulasta, Remicade, Avastin, Rituxan, Procrit, and Aranesp are almost entirely paid.

For this first edition, we surveyed 60 medical, pharmacy, and clinical directors representing 146 million lives to get an understanding of what payors are doing today and planning to do in the future to manage the quality and cost of care for medical benefit injectables. We then evaluated health plan medical benefit injectable claims such that benchmarks and trends could be determined.

ICORE Healthcare's mission has not changed in the past seven years: We serve as the center of medical injectable drug management. To this end, we believe this report is one additional resource to assist our customers, colleagues, and partners.

I want to give special thanks to the payors who served on our advisory board of this publication and who provided invaluable input into the report's overall objective, content, and design.

Most cordially,

Kjel A. Johnson, PharmD

EVOLUTION OF U.S. MARKET

2009 RANK[1]	OFF-PATENT	2012 RANK[†2]
Lipitor	2011	Nexium
Nexium	2014	Enbrel*
Plavix	2011	Neulasta
Advair	2011	Epogen
Seroquel	2011	Abilify
Abilify	2014	Remicade
Singulair	2010	Lovenox*
Actos	2011	Avastin
Enbrel*	2014	Rituxan
Epogen	2013	Cymbalta
Remicade	2018	Aranesp
Crestor	2016	Crestor
Avastin	2019	Humira*
Neulasta	2015	Vytorin
OxyContin	2013**	Procrit
Cymbalta	2013	Lantus*

yellow = oral; green = IV/IM/SQ; †No differential growth assumptions – straight removals of off-patent products; *Rx benefit; **One of three patents – one expires in 2013, while the remaining two expire in 2025.

[1] Bartholow M. Top 200 prescription drugs of 2009. *Pharmacy Times* website. http://www.pharmacytimes.com/issue/pharmacy/2010/May2010/RxFocusTopDrugs-0510. May 2010. Accessed October 8, 2010.
[2] ICORE Healthcare estimates

BY 2012,
11 of top 16
DRUGS WILL BE INJECTABLE OR INFUSIBLE
BY 2014, ALL
WILL LIKELY BE SPECIALTY

THUS, SPECIALTY DRUGS WILL COME TO DOMINATE THE PHARMACY MARKET

A SIGNIFICANT PORTION
>50%
ARE PAID UNDER THE MEDICAL BENEFIT

IN THE NEW MARKET,
Clinical Management
REQUIRES ABILITY TO WORK ON BOTH MEDICAL AND PHARMACY SYSTEMS

IN ADDITION, CURRENT BUSINESS MODELS ARE HEAVILY FOCUSED ON
PHYSICAL POSSESSION
AND DISPENSING OF DRUG – MORE CHALLENGING FOR PROVIDER-ADMINISTERED AGENTS

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A Benchmark for Medical Injectables

Today, every commercial payor in the U.S. is facing unmitigated increases in the cost of treating their members who require injectable biotech products; in fact, our experience with these payors suggests the trend ranges from 11 to 34%. Key cost drivers include: the expansion of indications for certain chemotherapies; the U.S. Food and Drug Administration (FDA) approval of several new therapies, such as Prolia, Provenge, and Jevtana; and price inflation, which most currently we estimate to be at 4%.

As a result, nearly every payor has thought through and implemented various cost-management strategies in the past few years. Interestingly, these cost managers have had few, if any, ways to benchmark their programs and results to that of other payors. We believe this report addresses this need.

The 2010 ICORE Healthcare Medical Injectables & Oncology Trend Report features two key sections: The first outlines our findings from the study of medical, pharmacy, and clinical directors at payors across the U.S. The section contemplates current and future cost-management techniques across six key medical injectable drug management drivers, as shown in the table below. Note that our findings for this section are generally reported as percentage of covered lives rather than percentage of payors to avoid bias, since nearly two-thirds of lives are covered under the top 10 payors.

The second key section of this report uses paid medical benefit claims to outline the spend and trend drivers of medical benefit injectables. In addition to these two sections, a review of the biosimilar and phase 2/3 pipelines are described, followed by a discussion of the key legislative outcomes in 2010.

Many of the benchmarks and statistics found in this report are not available elsewhere. Because of this, coupled with frequent requests from our customers and partners, you may access the report and selected data at **www.icorehealthcare.com/trends.aspx**

SIX KEY MEDICAL INJECTABLE DRUG MANAGEMENT DRIVERS

DRIVERS	HOW DO YOU KNOW IF YOUR STRATEGY IS WORKING?
Medical benefit drug formulary	Do you receive rebates, and can you improve drug mix?
Provider reimbursement	Does your approach reduce unit cost and improve mix?
Benefit design	Does your benefit plan change behavior or merely shift costs?
Distribution channel management	Are you able to optimize the use of low-cost distribution channels?
Utilization management (UM)	Do your UM functions support distribution and product preferences?
Operational improvements	What is your plan to correct systematic submission and payment errors?

2010 Report Methodology and Survey Demographics

The 2010 ICORE Healthcare Medical Injectables & Oncology Trend Report was developed with the guidance of our payor advisory board. Based on payor input, the report contains a combination of primary and secondary research methodologies.

The first section of the report was derived from a custom market research survey designed to gather feedback from health plan executives regarding how their organization operates around the six key medical injectable drug management drivers identified by ICORE Healthcare. The second section of the report was derived from secondary analyses of health plan paid claims data and illustrates the reality around what health plans actually pay for injectable and oncology drugs under their medical benefits.

LIMITATIONS OF THE DATA

As with any research, there are limitations to the data. Due to the expertise of the respondents required for the subject matter, the survey sample does not have the statistical properties of a random probability sample, though the sample was stratified based on plan size, national vs. regional focus, and geographic dispersion. While results may not be statistically projectable to the payor universe, they are descriptive and reflective of general market dynamics in that the survey reflects approximately two-thirds of the covered lives in the U.S. The secondary claims analyses are subject to the limitations of any secondary data set, namely that claims data are not outcomes data, for example, and they are subject to accuracy of diagnosis coding and other factors. A strength of the claims data set used in this report is that it is based on plans across the country and represents paid claims by the payor, rather than "billed" or "submitted" amounts, which are known to overestimate true costs of care.

HEALTH PLAN SURVEY METHODOLOGY

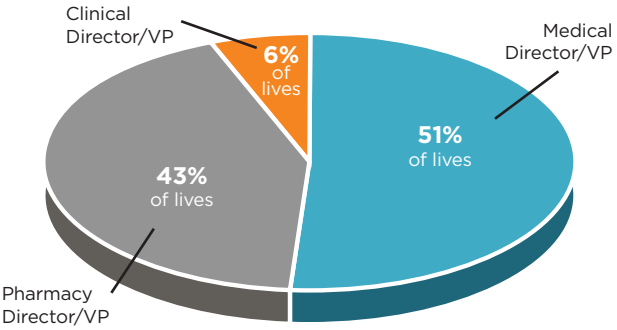
A sample of 160 U.S. commercial health plans was drawn from among the top payor organizations, based on number of lives covered. Survey topics were developed in conjunction with our payor advisory board and reflect common market-based management drivers. The survey questions were defined and programmed into a browser-based software program hosted on a secure server at Magellan Health Services, ICORE Healthcare's parent company. The survey was pretested and delivered to the sample audience by e-mail invitation. Following data collection, the results were validated, edited, and aggregated into data reported herein.

A total of 60 surveys were completed by health plan medical and pharmacy directors in the second quarter of 2010, representing a 37.5% response rate for this primary market research. As noted in the table below, survey respondents represented 60 distinct health plans that manage 146.3 million covered lives. In addition, the table on this page illustrates the completed survey respondent composition by number, plan size, and the corresponding percentages.

SURVEY RESPONDENT COMPOSITION

	COUNT	LIVES	% OF LIVES	% OF PLANS
Less than 500,000	26	4,992,000	3%	43%
500,000 to 999,999	15	9,669,750	7%	25%
1,000,000 to 4,999,999	15	46,630,000	32%	25%
5,000,000 or more	4	85,000,000	58%	7%
TOTAL	**60**	**146,291,750**	**100%**	**100%**

REPRESENTATION OF SURVEY RESPONDENTS



There was an equal split between the lives represented by medical directors (51%) and those in the pharmacy director/clinical director arena. Emergency medicine and family practice are the leading specialties reported by health plan medical directors. Further, survey respondents are experienced, with an average of 22 years in the field and eight years in their current position.

The survey results are primarily reported on a "percentage of lives" basis, which provides an indication of the marketplace impact of payor policies on the number of member lives, in addition to the "percentage of payors" incorporating any one policy. Further, in many cases, we have presented results stratified by the size of the health plan – less than 500,000 covered lives vs. 500,000 covered lives or more. In some instances, base sizes are small and caution should be used in interpretation of the data. Further, some percentages may add to slightly more or less than 100% due to rounding.

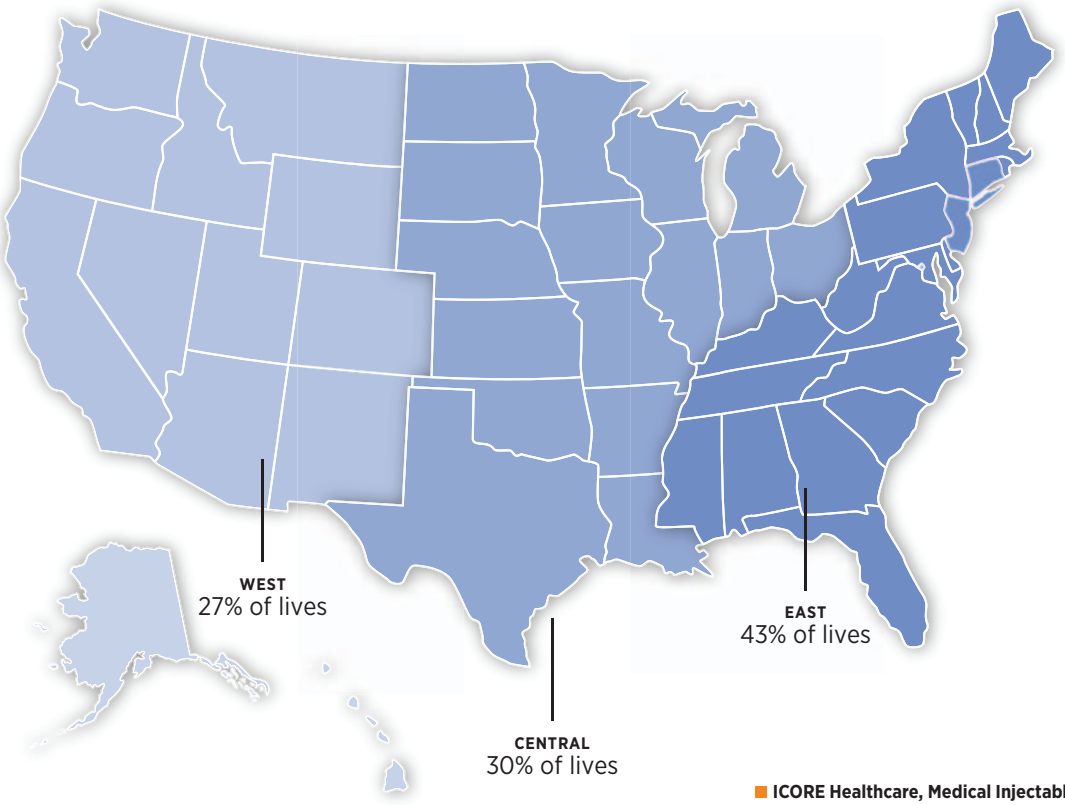
Survey respondents from national plans reflect 28% of the respondents, yet they cover 78% of the total lives in this survey. Conversely, regional plans have the larger percentage of payor respondents (72%), but reflect just 22% of the covered lives in the survey. There was a relatively even geographic split, with approximately one-third of the lives located in the East, Midwest, and West, respectively (see national map below).

Survey respondents noted that the majority of their members (73% of lives) are covered under mixed HMO/PPO products.

HEALTH PLAN CLAIMS DATA ANALYSES

ICORE Healthcare analyzed 2009 paid medical and pharmacy claims from a mix of national and regional health plans. The claims reflected predominantly commercial lives, followed by Medicare lives.

GEOGRAPHIC DISTRIBUTION OF LIVES AMONG REGIONAL PLANS



Report Summary and Conclusions

This 2010 ICORE Healthcare Medical Injectables & Oncology Trend Report evaluated injectable quality and cost management tools and trends of senior leaders from commercial payors and claims paid under the medical benefit.

Key findings of this report include:

- At least some medical injectable formulary management occurs at the vast majority of payors, with erythropoiesis-stimulating agents (ESAs) being the most common target.
- Plans representing over half the payors receive rebates for at least one injectable drug paid under the medical benefit. Rheumatoid arthritis drugs are most common, with Remicade as the market leader.
- For the most part, average wholesale price (AWP)-based reimbursement has been replaced by flat average sales price (ASP) reimbursement or variable fee reimbursement with larger plans favoring flat ASP methodologies.
- About two-thirds of commercial health plan members are subjected to coshares for medical injectables, and the average coshare amount is 17% of the drug cost. Half of those members are also subjected to copays.
- Relatively few lives (13%) are covered by payors who require only a copay for medical injectable products, and that copay averages $43.
- Nearly two-thirds of payors require genetic testing prior to receiving drugs such as Herceptin or Erbitux.
- All payors studied offer mammography and colorectal screening programs that aim to meet Healthcare Effectiveness Data and Information Set (HEDIS) measures; over half offer smoking cessation or prostate-specific antigen (PSA) testing programs. Compliance with these screening and prevention programs is highly variable, averaging 72%, 54%, 21%, and 17%, respectively.
- Medical injectables used to treat cancer account for over half of medical benefit injectable costs. A quarter of these costs are due to injectables used to treat autoimmune disorders, such as rheumatoid arthritis, Crohn's disease, and psoriatic arthritis. Oral chemotherapies, which are paid under the pharmacy benefit, account for about a tenth of the total cost of drugs used to treat cancer.
- Cost per claim varies widely for these products depending on where the site of service occurs. Medical injectables infused in a facility are about twice the cost of those that are administered in a provider's office.
- The association of medical injectable products with a number of different diagnoses varies widely; Avastin and intravenous immune globulin (IVIG) are the most likely products to be associated with a non-FDA-approved indication.

We know you will find this report novel and useful. Access the data at www.icorehealthcare.com/trends.aspx

PAYOR SURVEY DATA

Medical Benefit Drug Formulary

Recently, there has been an increase in the number of commercial health plans that have established medical benefit injectable drug formularies. In 2010, plans covering the majority of lives (75%) had formularies on the medical benefit and, in general, their network providers complied with such formularies. The likelihood of having a formulary was the same for smaller and larger payors, as defined by fewer than or at least 500,000 members, respectively. *See Figure 1, Medical Benefit Injectable Formularies in Place Overall, and Figure 2, Medical Benefit Injectable Formularies in Place by Size of Health Plan.*

FIG. 1 FORMULARIES IN PLACE OVERALL

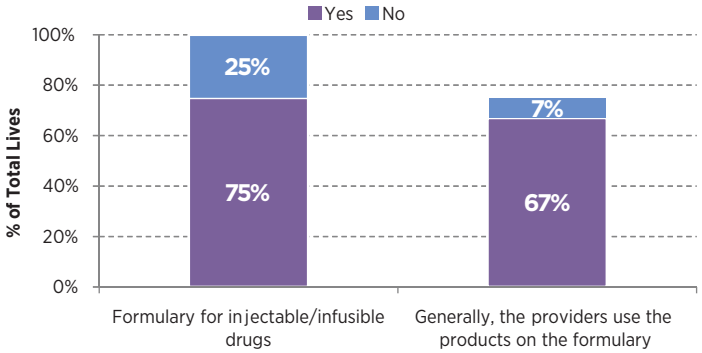


FIG. 2 FORMULARIES IN PLACE BY PLAN SIZE

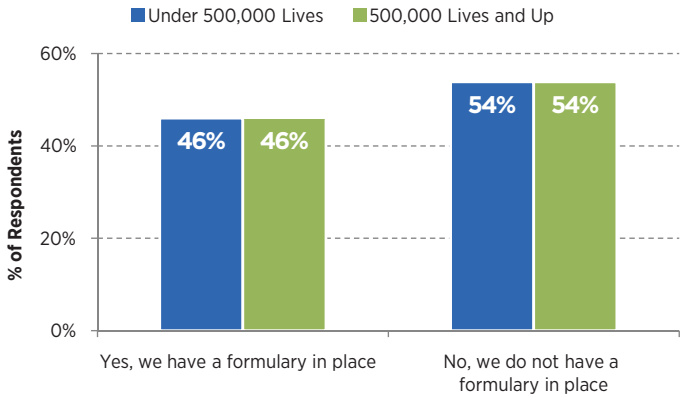
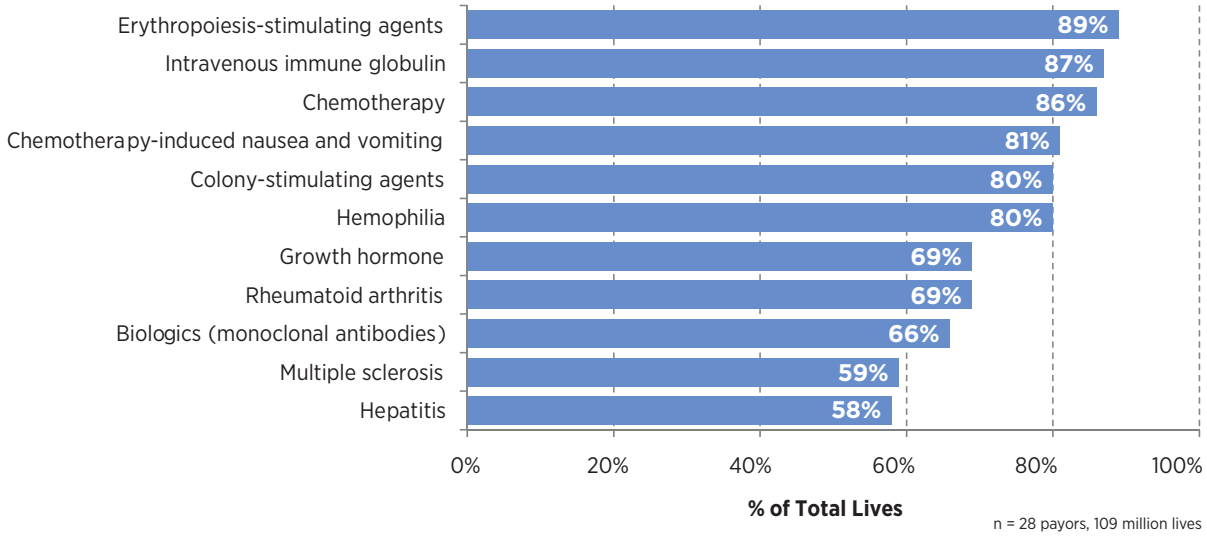


FIG. 3 THERAPEUTIC CLASSES WITH A MEDICAL FORMULARY CURRENTLY IN PLACE



n = 28 payors, 109 million lives

The medical formulary requirements that the health plan members were most likely to be subjected to were for (in decreasing order of likeliness): ESAs, a result of the Medicare regulations imposed a few years ago and a perception of product interchangeability; IVIG, because of the extent of off-label use and a perception of product interchangeability; and certain chemotherapies, because of the high cost of particular agents. *See Figure 3, Therapeutic Classes with a Medical Formulary Currently in Place.*

To further understand the extent to which formularies impact various chemotherapeutics, we identified cancers whose treatments were commonly under formulary management to some extent; seven were identified. *See Figure 4, Common Cancer Types Where Payors Have at Least Some Medical Drug Formulary in Place.*

FIG. 4 COMMON CANCER TYPES UNDER FORMULARY

CANCER TYPE	% OF LIVES
Non-small cell lung cancer	100%
Leukemia	63%
Metastatic breast cancer	63%
Renal cell carcinoma	63%
Prostate cancer	63%
Non-Hodgkin's lymphoma	63%
Multiple myeloma	63%

n = 12 payors, 94 million lives

Of the payors surveyed, plans representing more than half of the lives have a rebate contract for at least one injectable paid under the medical benefit. Larger plans were about 50% more likely to have established such a rebate program. This is likely to expand in the future as therapeutic areas such as rheumatology, immunology, and certain cancers have new market entries. It's also likely to expand as payors become more sophisticated in preferring drugs paid under the medical benefit and are therefore capable of moving market shares to preferred products. *See Figure 5, Rebates Received from Drug Manufacturers that Are Mainly Paid on the Medical Benefit Overall, and Figure 6, Rebates Received from Drug Manufacturers that Are Mainly Paid on the Medical Benefit by Size of Health Plan.*

The vast majority of commercial lives managed by payors who are receiving rebates for medical benefit injectables reportedly receive them for rheumatoid arthritis agents. Other therapies that are subject to rebates when paid under the medical benefit include ESAs and unspecified biologic agents. *See Figure 7, Therapeutic Classes Where Payors Receive Injectable/Infusible Product Rebates.*

FIG. 5 REBATES RECEIVED OVERALL

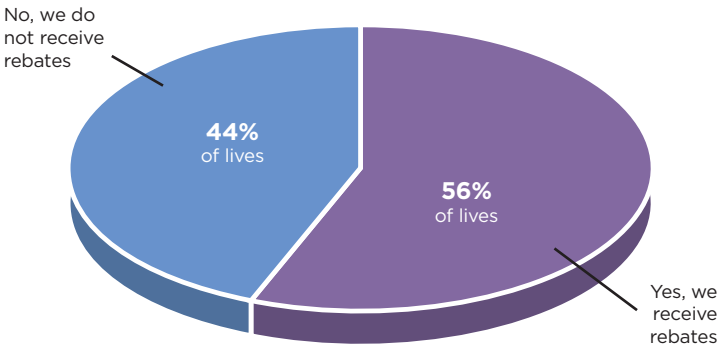


FIG. 6 REBATES RECEIVED BY SIZE OF HEALTH PLAN

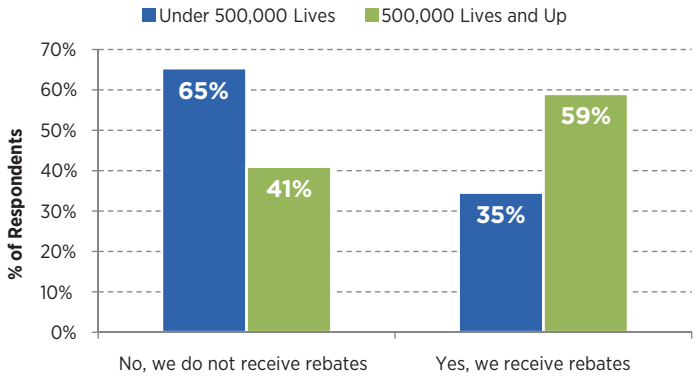
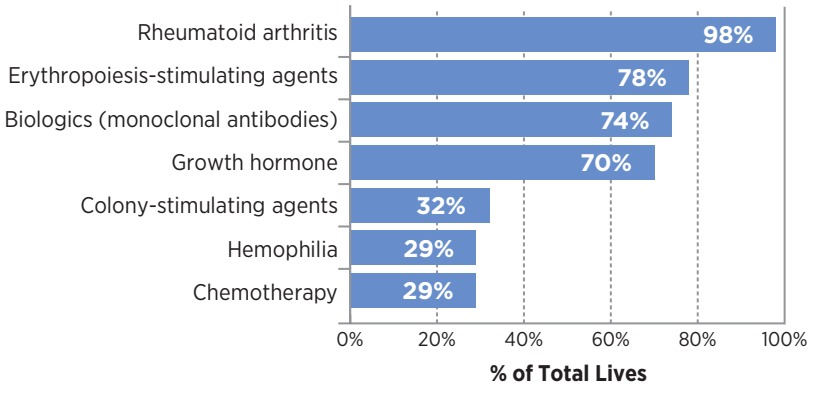


FIG. 7 THERAPEUTIC CLASSES WITH REBATES



n = 29 payors, 82 million lives

Provider Reimbursement

Medical benefit injectables are commonly purchased, prepared, and administered by providers and then billed for reimbursement of both drug and administration services through the patients' insurance carrier (commonly referred to as "buy & bill"). More than half of commercial lives are now covered by plans that reimburse for medical benefit injectables based upon ASP. About one in four lives is covered under reimbursement methodologies that use a variable fee schedule, or reference pricing. Few lives are reimbursing with the traditional AWP-minus, AWP-plus, or risk arrangement approaches. Smaller plans are more likely to use a variable fee schedule, while larger plans are more likely to use ASP-based reimbursement. *See Figure 8, Reimbursement Approach and the Extent of Discounts Used by Payors to Reimburse for Drugs Paid Under the Medical Benefit, and Figure 9, Reimbursement Approach and the Extent of Discounts Used by Payors to Reimburse for Drugs Paid Under the Medical Benefit by Size of Plan.*

Following the Medicare Modernization Act (MMA) of 2005, ICORE Healthcare has tracked a consistent migration of payors who have made the transition from reimbursing medical benefit injectables based upon AWP to those who use ASP-based methods. While you never get a 100% adoption of any one methodology, at this point, most of those that were going to move to an ASP-plus methodology have already done so.

Plan responses reflect the most common reimbursement strategy and may not necessarily reflect all reimbursement methodologies for a given plan.

FIG. 8 REIMBURSEMENT APPROACH

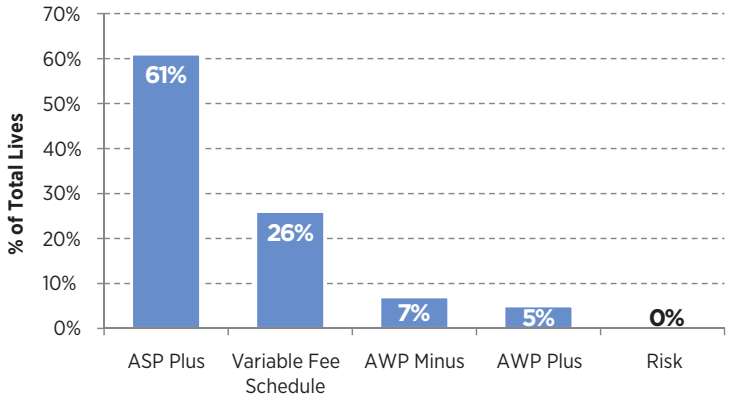
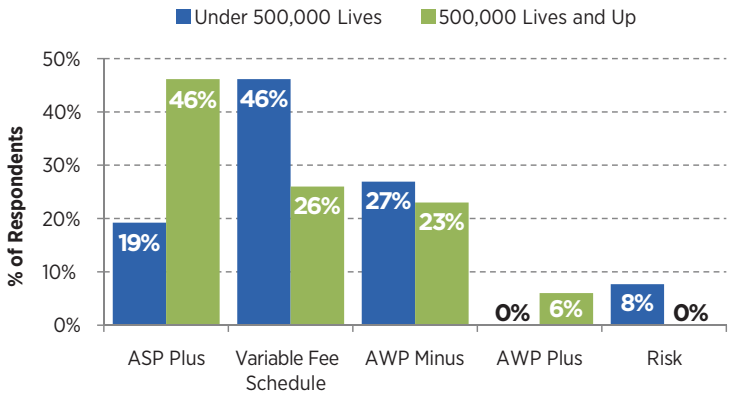


FIG. 9 REIMBURSEMENT APPROACH BY SIZE OF PLAN



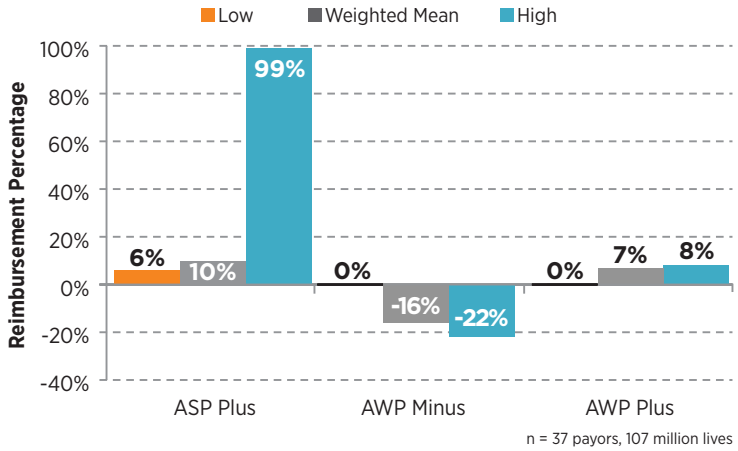
The level of ASP-plus reimbursement is most commonly associated with a 10% increase over ASP; AWP-minus reimbursement is most commonly associated with a 16% discount off of AWP.

At the time the MMA reimbursement changes occurred for Medicare patients, the Community Oncology Alliance (COA), a nonprofit organization dedicated to community oncology, stated that ASP+12% would be the minimum reimbursement to cover total cost of provider-administered drugs and acquisition costs.[3] Today, the average ASP-based reimbursement is below that threshold. *See Figure 10, Range of Reimbursement Methodology Percentage in Place for Injectables Paid Under the Medical Benefit.*

Commercial payors managing the vast majority of lives are developing their medical benefit drug reimbursement strategies utilizing internal resources. External vendors are also impacting reimbursement strategy development touching 21% of the lives, while just about one in 10 mimics the approach of the Centers for Medicare and Medicaid Services (CMS) of ASP+6%.

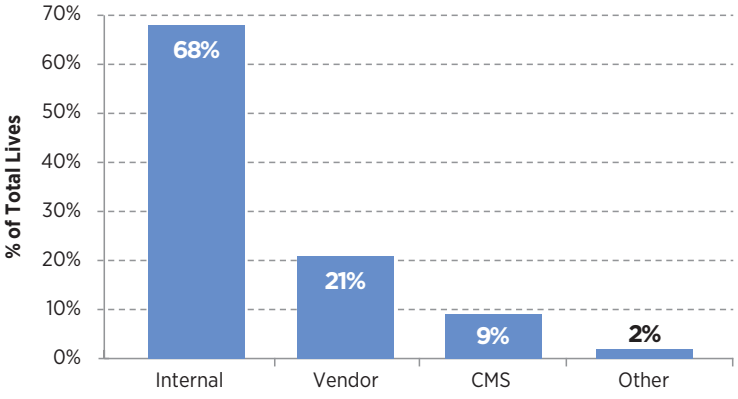
When internal development occurs, it is nearly always based upon a fixed percentage above or below the reference ASP or AWP. The risk of doing this with ASP is that it creates a "cost-plus" reimbursement strategy, which can, in turn, lead to the development of perverse incentives. *See Figure 11, How Payors Develop Their Medical Benefit Drug Reimbursement Strategies.*

FIG. 10 REIMBURSEMENT PERCENTAGE IN PLACE



n = 37 payors, 107 million lives

FIG. 11 DEVELOPMENT OF DRUG REIMBURSEMENT STRATEGIES



[3] Okon T, Coplon S, et al. Problems facing cancer care with Medicare's definition of average selling price. *Community Oncol.* 2004;1(1):59-63. http://www.communityoncology.net/journal/articles/0101059a.pdf. Accessed October 8, 2010.

Commercial health plans representing the vast majority of lives have not changed their medical benefit injectable reimbursement methodology in more than a year; this is a result of the early adopters of ASP-based reimbursement from 2005 to 2010. Moreover, the percentage modification to that strategy has not changed in the past year for the majority of member lives (61%), suggesting payors are not dissatisfied with their results following implementation of ASP-based methodologies. *See Figure 12, The Duration of Current Reimbursement Strategies at Health Plans.*

Ten percent of lives are subject to either capitated reimbursement and/or use case rate reimbursement for services. *See Figure 13, Portion of Payor Lives That Capitate Reimbursement to Providers or Use Case Rates.*

FIG. 12 DURATION OF CURRENT REIMBURSEMENT STRATEGIES

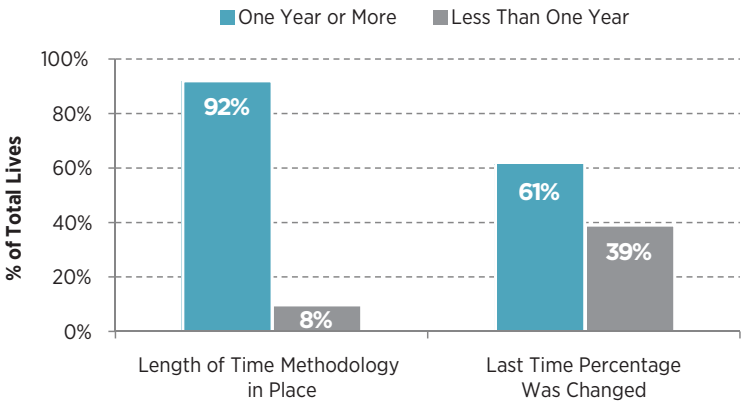
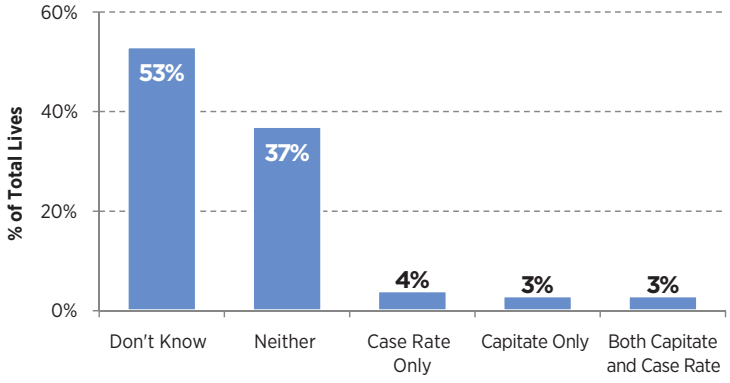


FIG. 13 PAYORS WHO CAPITATE OR USE CASE RATES



Benefit Design

About one-third of lives covered under commercial payors today are required to pay a coshare only; another one-third of lives may be subjected to both a copay or coshare, depending on what benefit design they are assigned by their employer. One-fourth of the lives are enrolled in a plan that requires neither a copay nor a coshare. *See Figure 14, Required Member Contribution for Injectables Paid Under the Medical Benefit Overall, and Figure 15, Required Member Contribution for Injectables Paid Under the Medical Benefit by Size of Plan.*

FIG. 14 MEMBERSHIP SUBJECT TO CONTRIBUTION

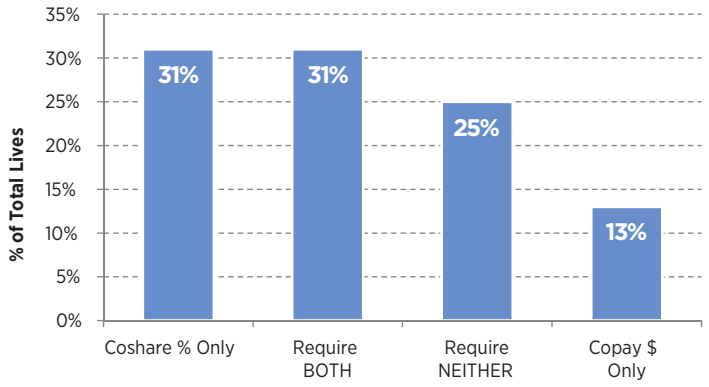
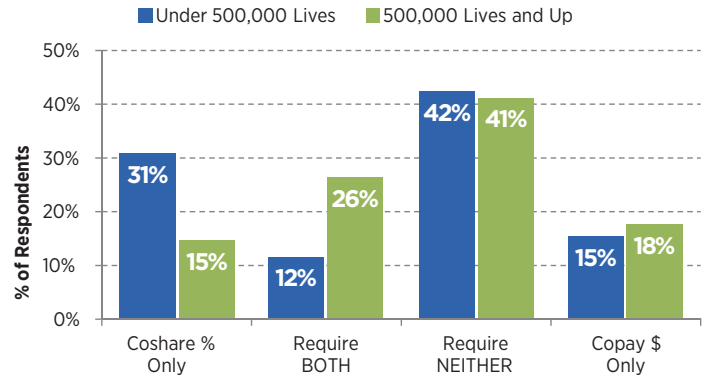


FIG. 15 MEMBER CONTRIBUTION BY SIZE OF PLAN

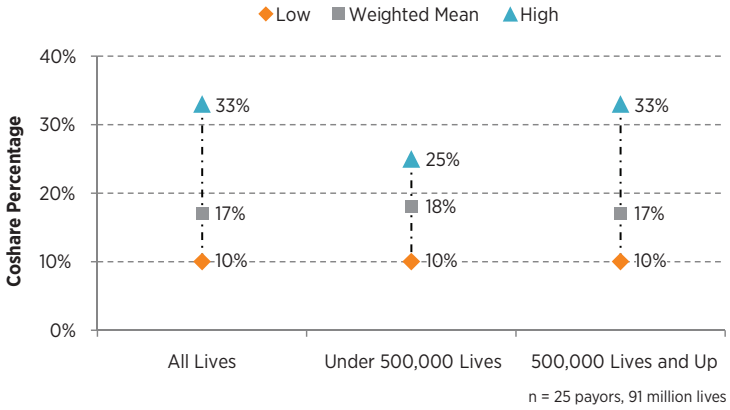


Coshares average approximately 17% of the cost of the therapy. This is fairly consistent regardless of plan size. *See Figure 16, Reported Coshare Amounts for Medical Benefit Injectables.*

For the lives that have a copay for medical benefit injectable drugs, members have a copay that averages $43. Insured lives covered under smaller plans were most likely to have lower copays for these injectables. *See Figure 17, Reported Copay Amounts for Medical Benefit Injectables.*

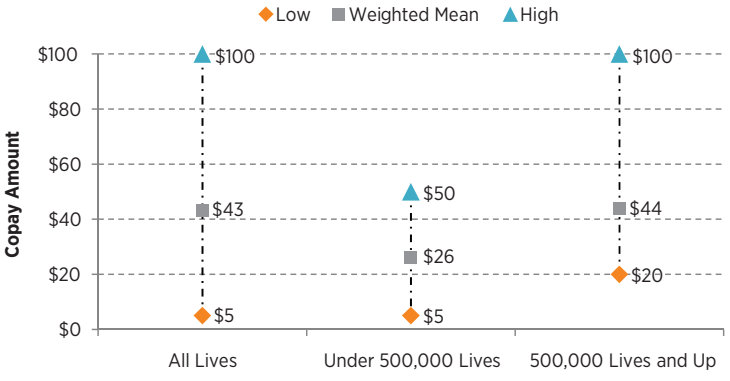
It is likely that copays of less than $100 are not influential, since many medical benefit injectable claims approach or exceed $5,000. *See Figure 50, Spend and Utilization per 1 Million Lives by Site of Service.* These copays would represent 2% or less of the true claim cost. Alternatively, our experience shows that when annual member contribution exceeds $2,500, demand falls. This suggests coshares without an out-of-pocket maximum may impair member compliance.

FIG. 16 REPORTED COSHARE AMOUNTS



n = 25 payors, 91 million lives

FIG. 17 REPORTED COPAY AMOUNTS



n = 23 payors, 64 million lives

In general, these plans do not offer different member cost share amounts across their service areas. This phenomenon was slightly more prevalent for relatively smaller payors. When this did occur, it was often the result of individual state operating differences. *See Figure 18, Variable Member Cost Share Requirements Across Different Plan Service Areas Overall, and Figure 19, Variable Member Cost Share Requirements Across Different Plan Service Areas by Size of Plan.*

FIG. 18 MEMBER COST REQUIREMENTS OVERALL

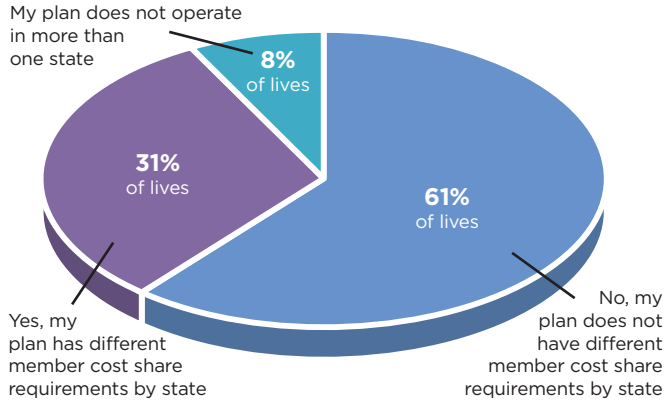
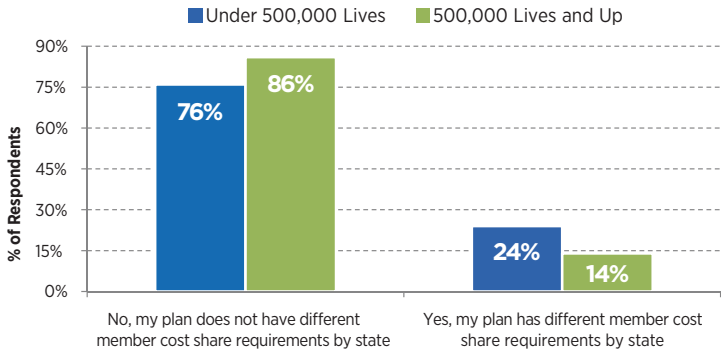


FIG. 19 MEMBER COST REQUIREMENTS BY PLAN SIZE



n = 40 payors, 134 million lives

There is a trend for commercial payors to subject more of their membership to coshares on medical injectables over time. Today, larger payors are more likely to have members with a medical benefit injectable coshare than smaller payors. Looking forward, payors intend to increase the percentage of members with a coshare by approximately 15%. *See Figure 20, Percentage of Member Lives Subject to a Coshare for Medical Injectables by Size of Plan.*

Of those payors reporting coshares for 2011, the projected percentage assigned to medical benefit injectables also slightly varies by plan size. This is relatively similar to the 17% average reported for 2010 (Figure 16); however, the ranges are wider, with some payors reporting up to a 55% member coshare. *See Figure 21, Reported Coshare Amounts for Medical Benefit Injectables in 2011.*

FIG. 20 MEMBERS SUBJECT TO A COSHARE BY SIZE OF PLAN

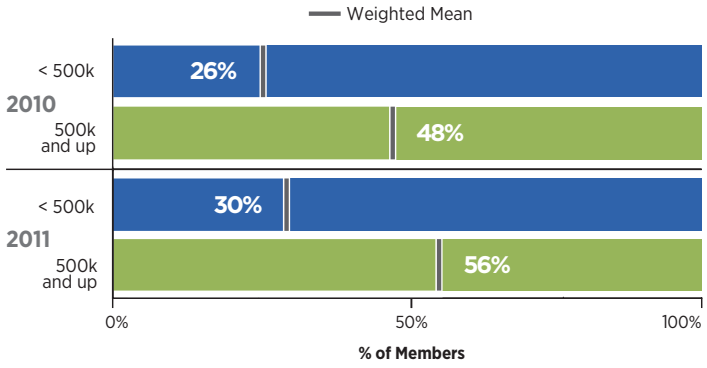
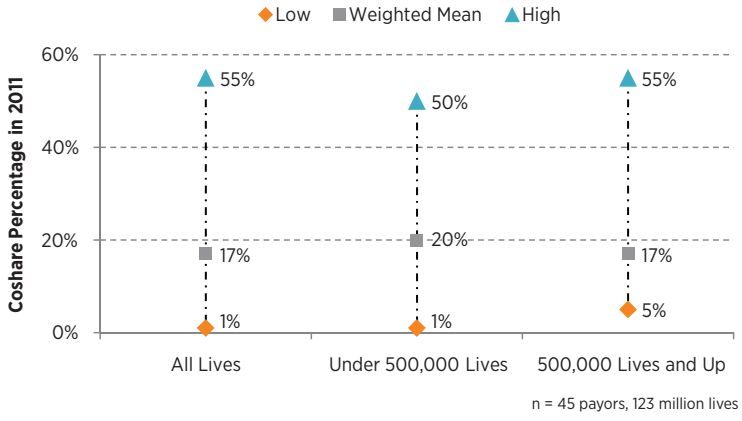


FIG. 21 COSHARE AMOUNTS PROJECTED FOR 2011



n = 45 payors, 123 million lives

Smaller payors report that the portion of their membership that has a medical benefit injectable copay will be reduced next year, while larger payors on average report no difference. *See Figure 22, Percentage of Members Subject to a Copay for Medical Injectables by Size of Plan.*

Of those payors reporting copays for 2011, the average amounts ranged from $4 to $100. Of note, the members within smaller health plans will be impacted by what appears to be a 40% copay increase for drugs under the medical benefit. *See Figure 23, Reported Copay Amounts for Medical Benefit Injectables in 2011.*

FIG. 22 MEMBERS SUBJECT TO A COPAY BY SIZE OF PLAN

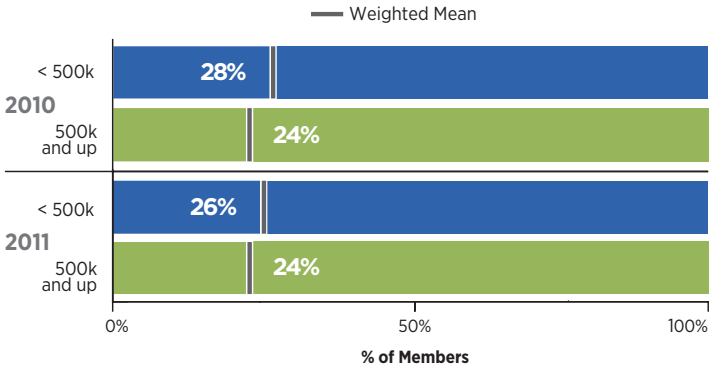
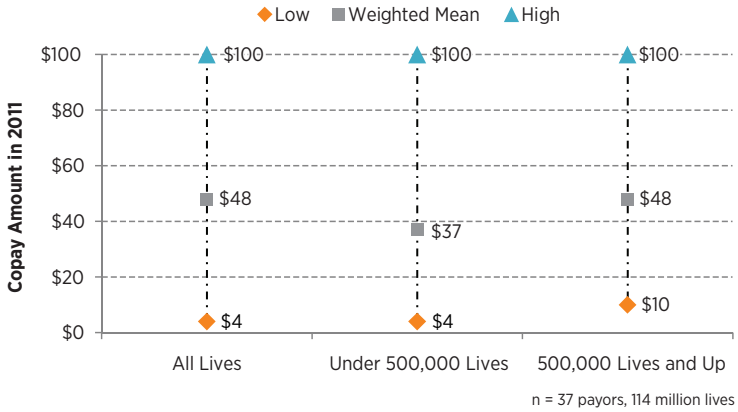


FIG. 23 COPAY AMOUNTS PROJECTED FOR 2011



n = 37 payors, 114 million lives

ORAL VS. INTRAVENOUS

About a quarter of covered member lives have parity across benefits in terms of member contribution, where the member contribution is equivalent regardless if the drug is paid under the medical or pharmacy benefit. Those payors who do not currently report parity commonly indicated that they were working toward this oral/IV member contribution parity for 2011. Some states already require this, for chemotherapies in particular. Ultimately, this will prevent member "benefit shopping" and will provide more consistent care across all administration channels. *See Figure 24, Member Contribution Parity Between IV and Oral Products with Similar Indications.*

Genomic testing is playing an increasingly important role in determining patient potential for positive treatment outcomes; therefore, payors are embracing the use of specific targeted genomic tests prior to chemotherapy selection in certain cancer types, primarily breast cancer and colorectal cancer. Half to two-thirds of payors require KRAS testing[4] and HER2 testing[5], which accounts for a majority of covered lives. Although just one in five payors requires Oncotype DX[6], they appear to be the larger plans because they account for one of every two lives. *See Figure 25, Genomic Test Requirements Before Chemotherapy.*

FIG. 24 MEMBER CONTRIBUTION PARITY

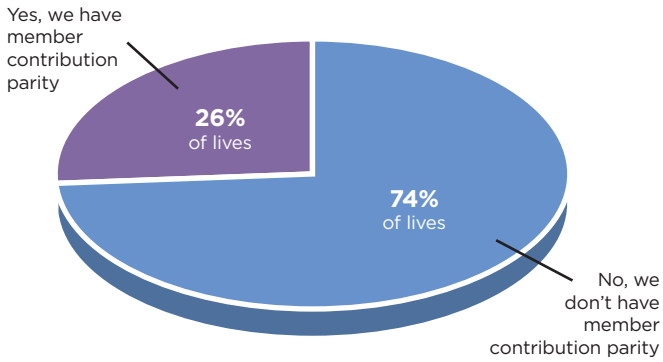
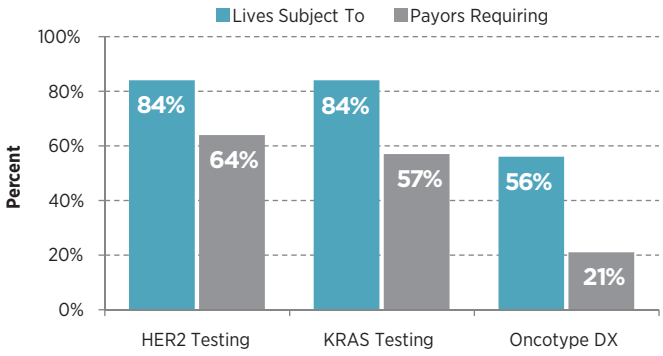


FIG. 25 GENOMIC TEST REQUIREMENTS



More information on these tests may be accessed at:

KRAS – www.kras-info.com
HER2 – www.herceptin.com/hcp/HER2-testing
Oncotype DX – www.oncotypedx.com

[4] KRAS (Kirsten RNA associated rat sarcoma 2 virus gene) testing is a new biomarker being used to select the best treatment for individual colorectal patients.

[5] HER2 (human epidermal growth factor receptor 2) testing is an important predictive and prognostic factor in breast cancer.

[6] Oncotype DX testing is a unique diagnostic test available to both breast cancer and colon cancer patients to help with treatment decisions.

Most members of commercial health plans (81% of covered lives) were enrolled in plans that featured established National Committee for Quality Assurance's HEDIS cancer screening/prevention programs. Breast and colorectal cancer screenings, along with medical assistance with smoking cessation, are part of the 2010 HEDIS measures.

Of those payors who have programs in place, colorectal and breast cancer screening programs were reported as available to all members, with prostate cancer detection and smoking-cessation programs also highly available to members. By and large, these prevention programs were developed by internal work teams. *See Figure 26, HEDIS Cancer Screening or Prevention Programs in Place, and Figure 27, Specific HEDIS Prevention Programs Established.*

FIG. 26 SCREENING OR PREVENTION PROGRAMS IN PLACE

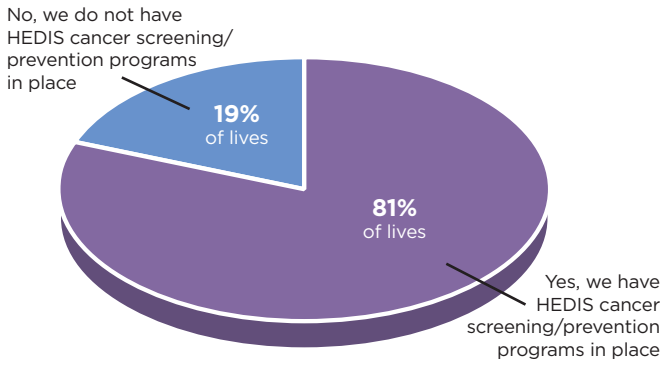
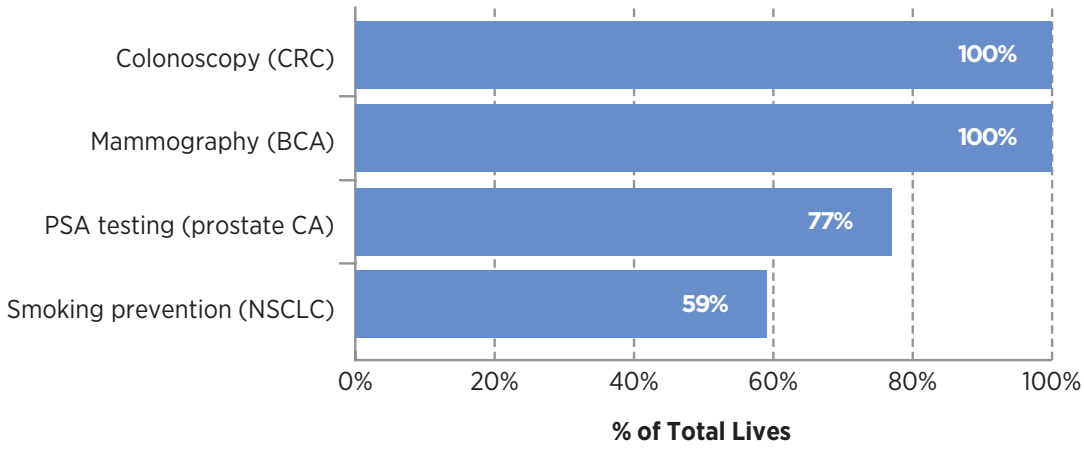


FIG. 27 HEDIS PREVENTION PROGRAMS ESTABLISHED



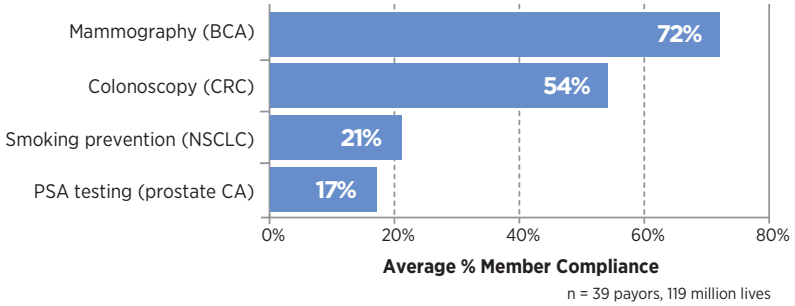
n = 39 payors, 119 million lives

Payors reported that members were most likely to have breast and colorectal cancer screenings performed, but they were unlikely to participate in other prevention initiatives. *See Figure 28, Most Recent Percentage of Member Compliance by Cancer Screening Program.*

Just 45% of covered members have end-of-life programs made available to them by the health plan, which includes a wide range of services: hospice, case management that focuses on social assistance for the member and family, education regarding palliative care, and prehospice programs. *See Figure 29, End-of-Life Programs Provided for Membership*.

Of these programs, few are covered as a separate benefit, as most are covered under the general medical benefit. For members receiving insurance from payors who have separate end-of-life benefits, the most common benefit offered is between 50 to 99 days of hospice care. *See Figure 30, End-of-Life Program Coverage.*

FIG. 28 MEMBER COMPLIANCE BY SCREENING PROGRAM



n = 39 payors, 119 million lives

FIG. 29 END-OF-LIFE PROGRAMS PROVIDED

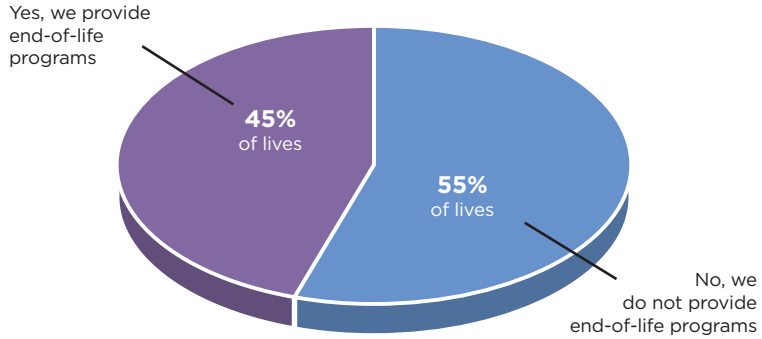
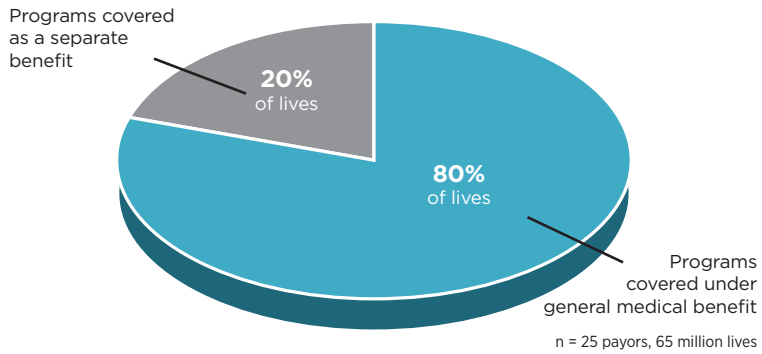


FIG. 30 END-OF-LIFE PROGRAM COVERAGE

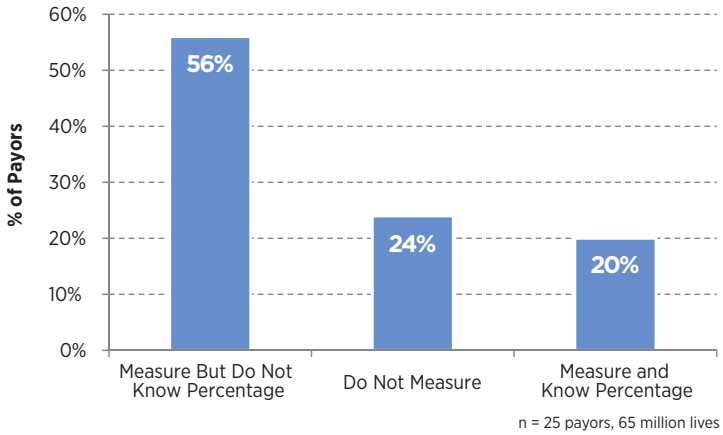


n = 25 payors, 65 million lives

Of those plans that offer end-of-life programs for their membership, three-fourths track the portion of eligible members who use these benefits, while only one in five payors, which represents just 2% of total lives, was able to provide the actual percentage. The self-reported average percentage of participation was just 10% among membership. *See Figure 31, Portion of Payors Who Know the Percentage of Eligible Members Who Actually Participated in These End-Of-Life Programs in the Last Year.*

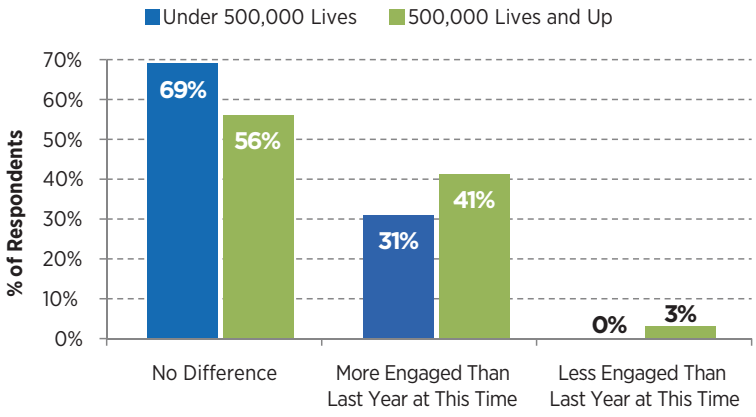
Employers are becoming a dominant force in benefit design, as virtually all respondents reported they are as engaged or more engaged than last year. Common requests received by health plans from employers regarding the management of medical benefit injectables include control of costs and trend, appropriate use, and use of benefit designs to manage costs. Questions regarding tier placement for specialty products were also common. *See Figure 32, Level of Employer Engagement with Health Plans in Developing Benefit Designs, by Size of Plan.*

FIG. 31 PAYORS MONITORING MEMBER PARTICIPATION



n = 25 payors, 65 million lives

FIG. 32 LEVEL OF EMPLOYER ENGAGEMENT BY PLAN SIZE



Distribution Channel Management

About half of all medical injectables are administered to members through the provider's office. Outpatient administration is used a fourth of the time, although this channel increased significantly during 2010. The home infusion channel represents about one-eighth of medical injectable claims and is primarily used for antibiotics, pain management, immune globulin, and factor administration. Few infused claims are distributed through the pharmacy benefit. The inpatient data was highly variable as the percentage of billed claims ranged from 0% to 40%. *See Figure 33, Average Percentage of Medical Injectable/Infusible Claims Billed from Each Site of Service.*

When providers administer medical injectables in their office, half are through a buy-and-bill process where the provider has purchased the drug and then invoices the payor. Specialty pharmacies provide approximately a fourth of the drugs to the provider's office for infusion. This process has several key challenges, including higher acquisition costs for the specialty provider and higher waste due to changes in dose, therapy, duration of therapy, and benefit and payor eligibility following shipment to the provider's office but prior to administration. *See Figure 34, Percentage of Medical Injectable/Infused Drug Volume Distributed to Members Through Various Billing Processes.*

FIG. 33 PERCENTAGE OF MEDICAL CLAIMS BILLED

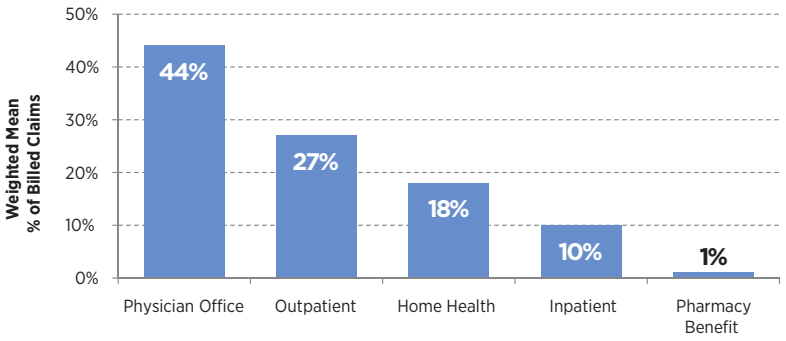


FIG. 34 DRUG VOLUME DISTRIBUTED TO PATIENTS VIA PHYSICIAN OFFICE

PRIMARY BILLING PROCESSES	WEIGHTED AVERAGE VOLUME
Buy and bill	50%
Specialty pharmacy provider	29%
Brown bag	11%
Mandatory vendor imposition	4%

Utilization Management

Most members of commercial plans (85%) are enrolled in plans that have implemented utilization management programs for certain provider-administered injectables. *See Figure 35, Managing Utilization of Injectable/Infusible Products Administered by a Provider.*

Prior authorization is the primary utilization management tool at health plans. Medical benefit injectables used to treat rheumatoid arthritis were the most managed, and IVIG, biologics, infused multiple sclerosis treatments, ESAs, and at least one chemotherapy were also subjected to prior authorization. Drugs used for chemotherapy that induce nausea and vomiting were exposed to the fewest management tools. *See Figure 36, Utilization Management Tools Used for Medical Injectable/Infusible Products in the Following Therapeutic Classes.*

FIG. 35 MANAGING UTILIZATION OF PRODUCTS

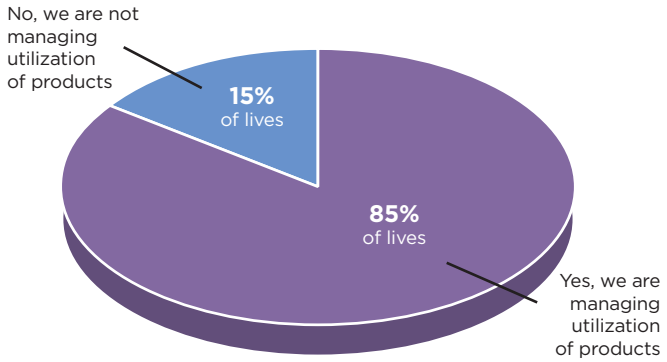


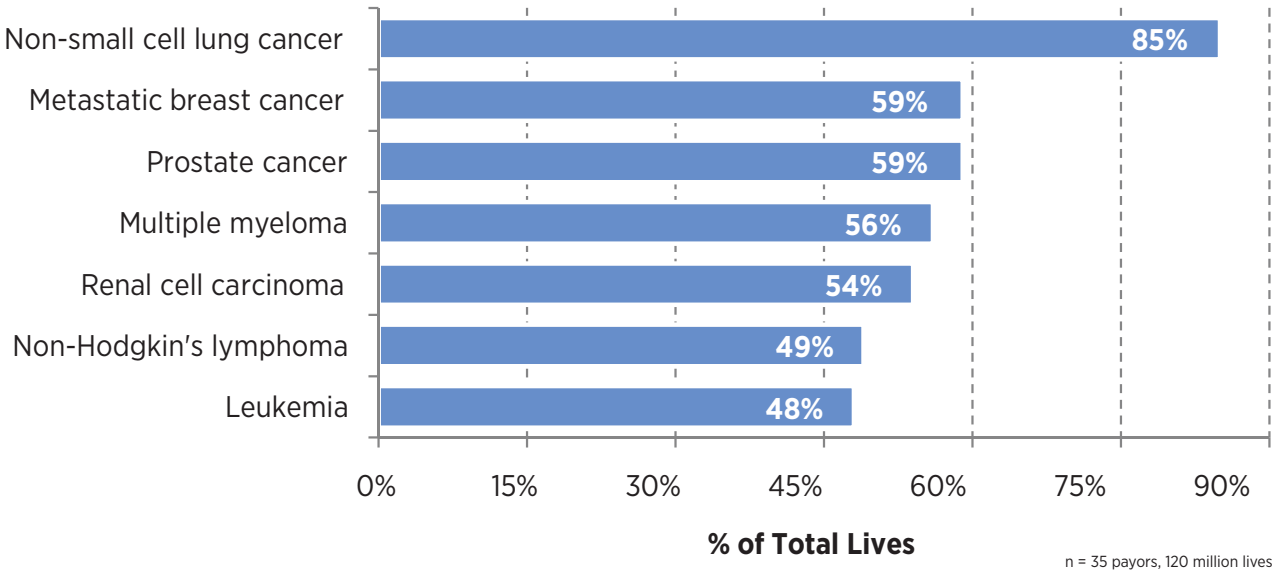
FIG. 36 UTILIZATION MANAGEMENT TOOLS BY CLASS

THERAPEUTIC CLASS	PRIOR AUTHORIZATION	DISEASE MANAGEMENT	STEP EDIT REQUIREMENTS	NCCN GUIDELINES	CASE MANAGEMENT	DIFFERENTIAL REIMBURSEMENT	NONE
Rheumatoid arthritis	91%	51%	55%	65%	57%	1%	1%
Intravenous immune globulin	68%	51%	16%	41%	33%	24%	1%
Biologics (monoclonal antibodies)	64%	51%	50%	38%	56%	1%	0%
Multiple sclerosis	64%	53%	21%	42%	56%	28%	1%
Erythropoiesis-stimulating agents	54%	52%	39%	43%	31%	25%	5%
Chemotherapy	51%	52%	12%	63%	48%	2%	4%
Colony-stimulating agents	49%	27%	34%	66%	31%	25%	10%
Hemophilia	28%	52%	10%	35%	63%	54%	12%
Chemotherapy-induced nausea and vomiting	22%	27%	15%	9%	32%	25%	15%

n = 43 payors, 125 million lives

Non-small cell lung, breast, and prostate cancers are some of the most common cancer diagnoses found in commercial payors. As a result, these cancers were commonly subjected to utilization management tools. Renal cell cancers and multiple myeloma were also frequently managed, as a result of the availability of oral therapies and the ease of management on the pharmacy benefit. Prior authorization, National Comprehensive Cancer Network (NCCN)[7] guideline adherence, edits, genetic testing, and retrospective drug utilization review were common verbatim mentions regarding how payors accomplish this. *See Figure 37, Cancer Types Most Commonly Subjected to Medical Utilization Tools.*

FIG. 37 CANCERS SUBJECTED TO MEDICAL UTILIZATION TOOLS



n = 35 payors, 120 million lives

[7]More information regarding NCCN can be found at www.nccn.org.

Avastin, Cerezyme, Erbitux, Eloxatin, Abraxane, and Aloxi were all subjected to prior authorization in commercial plans covering more than half of the member lives. Few payors have no medical injectable management tools or controls in place. *See Figure 38, Management Tools Used for Common Medical Injectable Therapies.*

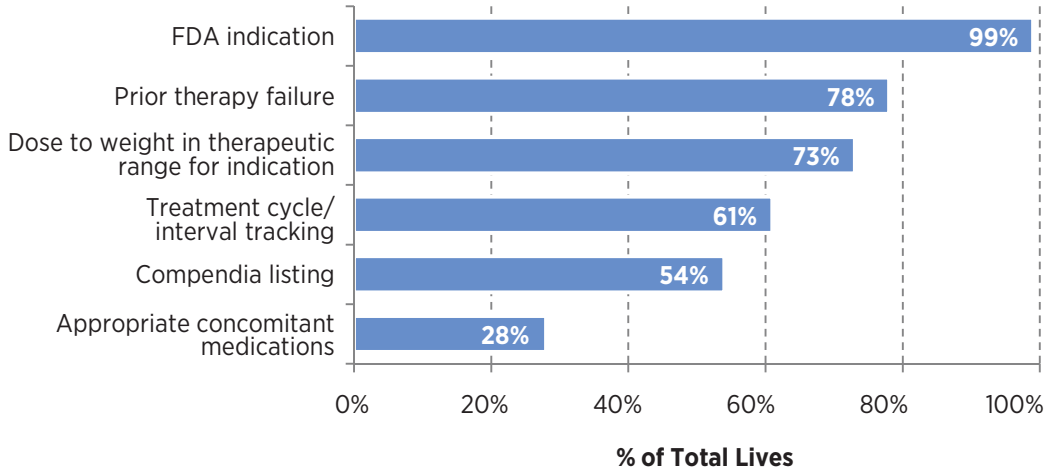
Commercial payors managing the vast majority of lives are using FDA indication when developing authorization criteria. Plans representing about three-fourths of the covered lives also have a policy to approve a medical injectable drug if the member has failed the medication in the past. *See Figure 39, Specific Prior Authorization Criteria That May Be Required.*

FIG. 38 MANAGEMENT TOOLS FOR COMMON THERAPIES

DRUGS	PRIOR AUTHORIZATION	DISEASE MANAGEMENT	STEP EDIT REQUIREMENTS	NCCN GUIDELINES	CASE MANAGEMENT	DIFFERENTIAL REIMBURSEMENT	NONE
Cerezyme	66%	51%	10%	31%	40%	25%	9%
Avastin	65%	51%	12%	34%	38%	25%	9%
Erbitux	65%	51%	10%	32%	34%	25%	9%
Eloxatin	62%	51%	10%	30%	34%	25%	11%
Abraxane	59%	51%	11%	33%	34%	25%	10%
Aloxi	55%	51%	13%	31%	34%	25%	11%
Herceptin	34%	51%	34%	34%	34%	25%	9%
Taxotere	33%	51%	10%	33%	34%	1%	11%
Remicade	31%	52%	47%	31%	32%	25%	8%
Rituxan	31%	51%	37%	31%	34%	25%	9%

n = 43 payors, 125 million lives

FIG. 39 SPECIFIC PRIOR AUTHORIZATION CRITERIA



n = 39 payors, 85 million lives

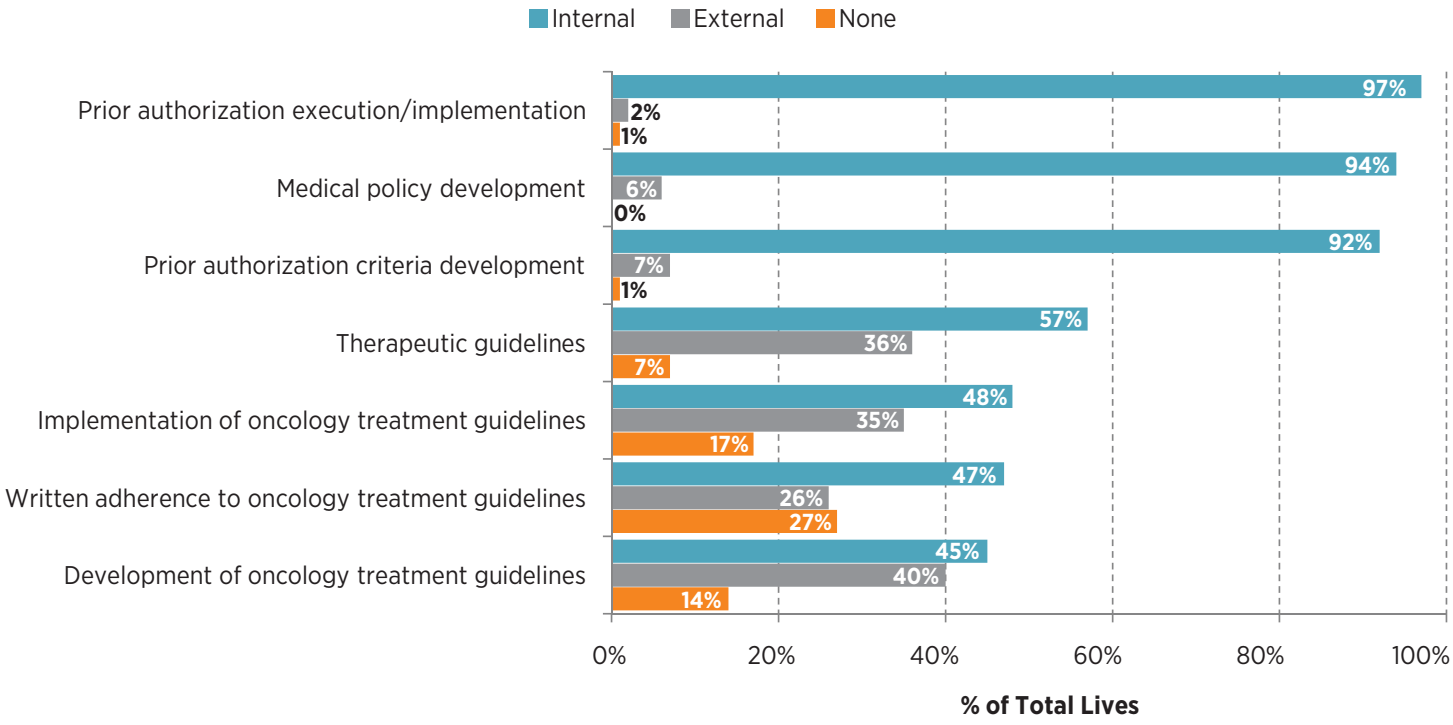
When asked about the greatest medical injectable threat in 2011, one-third of payors mentioned overall cost. Appropriate utilization, chemotherapy drugs overall, and number of drugs in the approval pipeline with minimal expected improvements in efficacy were mentioned by 10 to 20% of payors. *See Figure 40, Top Medical Injectable Concerns in 2011.*

For the most part, prior authorization, coverage policies, and criteria were developed internally by payors representing the vast majority of lives. Treatment guidelines and programs around those guidelines were commonly developed by external agencies – predominantly by the NCCN, which is an alliance of 21 of the world's leading cancer centers. *See Figure 41, Where Management Services Are Developed at Health Plans.*

FIG. 40 TOP MEDICAL INJECTABLE CONCERNS (2011)

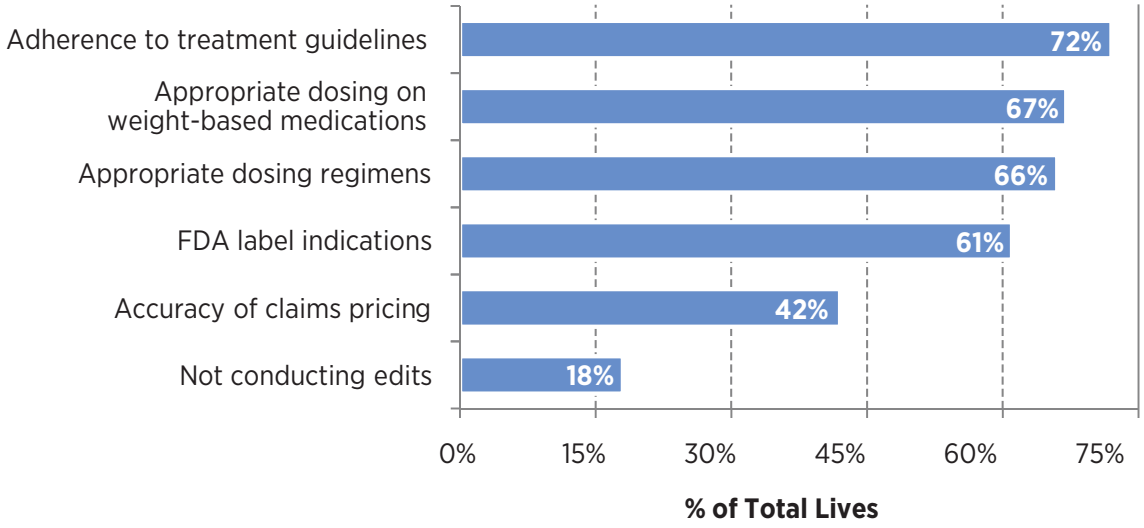
MEDICAL INJECTABLE CONCERN	% OF PAYORS
Overall Cost	32%
Appropriate Utilization	20%
Chemotherapy Drugs Overall	15%
Number of Drugs in Pipeline with Minimal Improved Efficacy	13%
Price Increases	8%
Expansion on Drug Indications	3%
IVIG	2%
Third-Line-Plus Chemotherapy	2%

FIG. 41 WHERE MANAGEMENT SERVICES ARE DEVELOPED



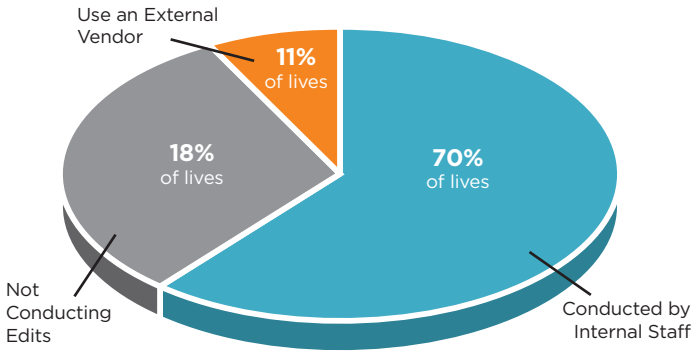
Operational Improvements

FIG. 42 POST-HOC EDITS CONDUCTED



Payors are conducting various post-payment edits for provider-administered injectables paid on a member's medical benefit. Specifically, these include guidelines (predominantly NCCN), appropriateness of dose and duration edits, and edits that mitigate off-label use. Commonly these edits are developed by internal staff and then implemented internally through existing claims-editing software. Approximately two-thirds of covered lives are enrolled in plans that do this internally, while less than one in five covered lives is subjected to no medical benefit injectable edits. *See Figure 42, Post-Hoc Edits Conducted on Medical Injectable Claims, and Figure 43, Implementation of Edits.*

FIG. 43 IMPLEMENTATION OF EDITS



HEALTH PLAN CLAIMS DATA

Trend Drivers

Based on paid claims analyses, as a general guideline, one can expect that a 1-million-life commercial plan would average approximately $83 million in medical benefit injectable costs in 2009. Of that, the top 25 medical drugs comprised more than 80% of the total medical injectable spend, with Remicade being the largest number of paid units and overall spend per 1 million commercially insured lives.

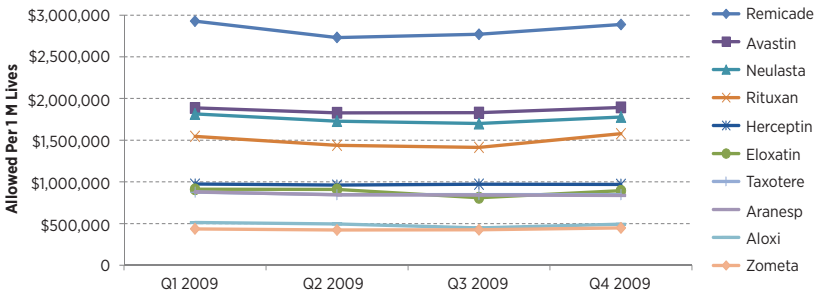
For the top 10 drugs responsible for more than 50% of the overall medical injectable benefit spend, there were no differences in spend per quarter for any drug during 2009. This existed for several reasons – while unit cost increased, many of the payors in this study were relatively aggressive users of utilization management, reducing number of units and thus flattening the trend. Examples include self-injectable first programs that reduce Remicade use, prior authorization of Avastin, HER2 testing for Herceptin, and drug mix improvements for taxanes and antiemetic drugs. Although the first and fourth quarters were generally associated with greater spend per quarter than the second and third quarters, this increase was not significant and was likely due to yearly benefit timing.

Eloxatin, which faced generic alternative entry in 2009, will likely trend downward once generic acquisition pricing becomes incorporated into the ASP. Other key medical injectable drugs will face patent expiration and generic competition in the foreseeable future, further reducing the cost trends of these individual products. Overall trend is expected to continue to rise due to expanded indications, new market entries, and pending utilization growth due to healthcare reform. *See Figure 44, Top 25 Medical Injectable Drugs by Allowed Amount per 1 Million Lives, and Figure 45, Top 10 Drugs by Quarter (2009).*

FIG. 44 TOP 25 MEDICAL INJECTABLE DRUGS (2009)

DRUG	RANKING	J CODE	UNITS PER 1 M LIVES	CALCULATED COST PER UNIT	ALLOWED PER 1 M LIVES
Remicade	1	J1745	176,801	$64	$11,319,516
Avastin	2	J9035	123,003	$60	$7,439,946
Neulasta	3	J2505	1,837	$3,823	$7,023,023
Rituxan	4	J9310	10,317	$579	$5,977,651
Herceptin	5	J9355	58,157	$67	$3,877,448
Eloxatin	6	J9263	331,455	$11	$3,525,041
Taxotere	7	J9170	8,849	$386	$3,418,043
Aranesp	8	J0881	890,540	$4	$3,405,312
Aloxi	9	J2469	72,887	$26	$1,918,375
Zometa	10	J3487	7,307	$237	$1,733,124
Orencia	11	J0129	80,464	$21	$1,723,889
Alimta	12	J9305	32,874	$52	$1,696,061
Gemzar	13	J9201	11,405	$147	$1,672,254
Procrit	14	J0885	116,661	$12	$1,348,129
Erbitux	15	J9055	24,122	$53	$1,280,052
Velcade	16	J9041	31,081	$38	$1,177,300
Tysabri	17	J2323	131,951	$9	$1,173,087
Abraxane	18	J9264	103,066	$10	$1,023,218
Sandostatin	19	J2353	8,204	$122	$1,004,596
Gammagard	20	J1566	22,426	$42	$940,721
Eligard	21	J9217	2,671	$286	$762,708
Carboplatin	22	J9045	13,722	$53	$722,316
Taxol	23	J9265	10,550	$64	$675,147
Gammagard	24	J1569	9,662	$60	$582,358
Soliris	25	J1300	2,152	$194	$418,141

FIG. 45 TOP 10 DRUGS BY QUARTER



When the diagnosis codes used for members who receive medical benefit injectable drugs were reviewed, only 23 diagnoses represent 1% or more of patients receiving medical injectables. The top 15 diagnoses accounted for 50% of total patients per million lives, with five of the top six ICD-9 codes for rheumatologic disorders. *See Figure 46, Portion of Health Plan Members Who Received a Medical Injectable for Key Diagnoses.*

FIG. 46 PORTION OF MEMBERS WHO RECEIVED A MEDICAL INJECTABLE

RANKING	PRIMARY DIAGNOSIS CODE	PRIMARY DIAGNOSIS CODE DESCRIPTION	% OF TOTAL PATIENTS PER 1 M LIVES
1	715	Osteoarthrosis	8%
2	726	Peripheral enthesopathies	7%
3	719	Disorders of joint	7%
4	724	Disorders of back	4%
5	786	Symptoms involving respiratory system	3%
6	727	Disorders of synovium, tendon, and bursa	3%
7	466	Acute bronchitis and bronchiolitis	2%
8	714	Rheumatoid arthritis	2%
9	174	Breast cancer	2%
10	728	Disorders of muscle, ligament, and fascia	2%
11	787	Symptoms involving digestive system	2%
12	281	Other deficiency anemias	2%
13	477	Allergic rhinitis	2%
14	266	Deficiency of B-complex components	2%
15	729	Disorders of soft tissues	2%
16	493	Asthma	2%
17	692	Contact dermatitis and other eczema	1%
18	722	Intervertebral disc disorders	1%
19	780	General symptoms	1%
20	723	Disorders of cervical region	1%
21	789	Symptoms involving abdomen and pelvis	1%
22	733	Osteoporosis	1%
23	280	Iron deficiency anemias	1%

Spend Drivers

Injectable chemotherapy, as expected, represents more than one-third of all medical injectable costs; when chemotherapy support medicines are considered, injectables associated with cancer care represent just more than half of medical injectable costs. For reference purposes as depicted in Figure 47, a 1-million-life commercial payor in 2009 spent, on average, almost $4 million on oral chemotherapy, but spent nearly $32 million on injectable chemotherapies, suggesting that oral chemotherapy is approximately 11% of a payor's total chemotherapy spend. There are several key factors for this: the provider and patient interests in office-based administration, relatively few cancers with oral chemotherapy options, and the much more aggressive management performed on pharmacy benefit chemotherapies when compared with injectable chemotherapies paid under the medical benefit.

Provider-administered injectables used to treat rheumatologic disorders represent the second largest therapeutic area by spend – nearly 25% of total medical injectable costs.

IVIG costs payors approximately $2.2 million for each 1 million insured commercial lives. Importantly, this is roughly one-third of the spend, with another several million administered through home infusion and the final one-third administered through the specialty pharmacy channel. *See Figure 47, Spend by Key Therapeutic Class per 1 Million Lives.*

FIG. 47 SPEND BY KEY THERAPEUTIC CLASS

THERAPEUTIC CLASS	ALLOWED PER 1 M LIVES	% OF TOTAL SPEND
IV chemotherapy	$31,572,798	38%
Rheumatory	$19,021,848	23%
Granulocyte colony-stimulating factor	$8,093,891	10%
Erythropoiesis-stimulating agent	$4,753,441	6%
Intravenous immune globulin	$2,205,164	3%
Oral chemotherapy	$3,971,891	5%
Grand Total	**$69,619,033**	**84%**

National Trends

When the specialty of prescribing providers is reviewed, four specialists represent more than three-fourths of the medical benefit injectable spend: hematologists, oncologists, rheumatologists, and urologists. The list of other provider specialties is extensive and includes gastroenterologists, pediatricians, ophthalmologists, gynecologists, and others. *See Figure 48, Spend per 1 Million Lives by Provider Specialty, and Figure 49, Claims per 1 Million Lives by Provider Specialty.*

Medical benefit injectables are administered primarily through one of three channels: the hospital, home infusion, or the provider's office. As shown for the top 10 drugs by annual cost, the hospital channel is consistently more costly than other channels and generally costs twice what a provider-administered injectable given in the provider's office would cost. In 2010, there has been a trend toward providers administering injectables in the facility outpatient channel rather than in their offices, which will significantly increase costs of care over time. *See Figure 50, Spend and Utilization per 1 Million Lives by Site of Service.*

FIG. 48 SPEND BY PROVIDER SPECIALTY

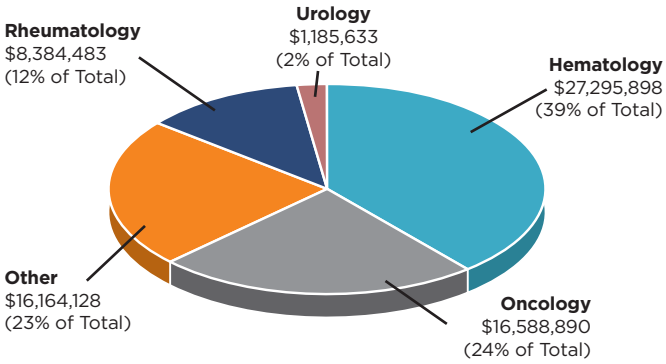


FIG. 49 CLAIMS BY PROVIDER SPECIALTY

SPECIALTY	UNITS PER 1 M LIVES (% OF TOTAL)	CLAIMS PER 1 M LIVES (% OF TOTAL)
Hematology	1,379,225 (46%)	45,282 (42%)
Oncology	850,288 (29%)	29,439 (28%)
Other	557,765 (19%)	19,948 (19%)
Rheumatology	163,176 (5%)	8,301 (8%)
Urology	32,378 (1%)	3,707 (3%)
Grand Total	**2,982,832**	**106,677**

FIG. 50 SPEND AND UTILIZATION PER 1 MILLION LIVES BY SITE OF SERVICE

RANKING	J CODE	BRAND NAME	ALLOWED PER 1 M LIVES	UNITS PER 1 M LIVES	CALCULATED UNIT RATE	$/CLAIM	UNITS/ CLAIM	$/CLAIM		
								HOSPITAL	HOME INFUSION	MEDICAL OFFICE
1	J1745	Remicade	$11,319,516	176,801	$64	$4,608	43	$5,995	$3,255	$3,221
2	J9035	Avastin	$7,439,946	123,003	$60	$5,928	58	$8,832	N/A	$3,024
3	J2505	Neulasta	$7,023,023	1,837	$3,823	$4,526	1	$5,971	$3,410	$3,081
4	J9310	Rituxan	$5,977,651	10,317	$579	$6,816	8	$9,068	N/A	$4,565
5	J9355	Herceptin	$3,877,448	58,157	$67	$3,514	34	$4,877	N/A	$2,150
6	J9263	Eloxatin	$3,525,041	331,455	$11	$5,249	323	$6,822	N/A	$3,677
7	J9170	Taxotere	$3,418,043	8,849	$386	$3,689	6	$5,090	N/A	$2,287
8	J0881	Aranesp	$3,405,312	890,540	$4	$1,578	233	$2,080	N/A	$1,077
9	J2469	Aloxi	$1,918,375	72,887	$26	$444	10	$586	$489	$303
10	J3487	Zometa	$1,733,124	7,307	$237	$2,818	27	$4,169	$2,679	$1,607

When reviewing medical benefit injectable drugs that are most commonly used for multiple indications, wide variations in those indications were found. The table below lists the top five diagnoses for Avastin, Herceptin, IVIG, Orencia, Remicade, and Rituxan. Of interest, Herceptin and Orencia had the fewest nonprimary indication uses, and Avastin had the most diagnosis variability. IVIG (generic and brand) was most commonly used for neurological disorders, including neuropathy and multiple sclerosis. A study of IVIG has shown more than 80% of use is for non-FDA-approved indications. *See Figure 51, Top Five Diagnosis Codes for Key Medical Benefit Drugs.*

FIG. 51 TOP FIVE DIAGNOSIS CODES

AVASTIN

DESCRIPTION	CODE	$/1 M LIVES	CLAIMS PER 1 M LIVES
Malignant neoplasm of colon	153	$471,694	136
Malignant neoplasm of lung	162	$401,172	66
Breast cancer	174	$379,548	81
Malignant neoplasm of rectum	154	$155,271	45
Malignant neoplasm of ovary	183	$68,066	14

ORENCIA

DESCRIPTION	CODE	$/1 M LIVES	CLAIMS PER 1 M LIVES
Rheumatoid arthritis	714	$374,846	223
Psoriasis and similar disorders	696	$2,109	1
Other and unspecified arthropathies	716	$1,831	1
Disorders of back	724	$1,774	1
Deficiency of B-complex components	266	$1,553	1

HERCEPTIN

DESCRIPTION	CODE	$/1 M LIVES	CLAIMS PER 1 M LIVES
Breast cancer	174	$836,371	390
Encounter for other and unspecified procedures and aftercare	V58	$17,211	9
Personal history of malignant neoplasm	V10	$7,021	5
Carcinoma in situ of breast and genitourinary system	233	$6,493	3
Malignant neoplasm of pancreas	157	$4,308	5

REMICADE

DESCRIPTION	CODE	$/1 M LIVES	CLAIMS PER 1 M LIVES
Rheumatoid arthritis	714	$1,468,642	465
Regional enteritis	555	$480,140	141
Psoriasis and similar disorders	696	$428,949	119
Ulcerative colitis	556	$175,171	51
Ankylosing spondylitis and other inflammatory spondylopathies	720	$118,383	35

IVIG

DESCRIPTION	CODE	$/1 M LIVES	CLAIMS PER 1 M LIVES
Inflammatory and toxic neuropathy	357	$177,310	41
Multiple sclerosis	340	$103,798	28
Disorders involving the immune mechanism	279	$85,066	27
Hereditary and idiopathic peripheral neuropathy	356	$79,660	26
Myoneural disorders	358	$53,493	10

RITUXAN

DESCRIPTION	CODE	$/1 M LIVES	CLAIMS PER 1 M LIVES
Other malignant neoplasms of lymphoid and histiocytic tissue	202	$681,857	159
Rheumatoid arthritis	714	$224,741	38
Lymphoid leukemia	204	$140,309	32
Lymphosarcoma and reticulosarcoma	200	$133,875	30
Purpura	287	$56,720	13

PRODUCT PIPELINE AND LEGISLATIVE TRENDS

Drug Pipeline

Several very costly medical injectables were approved in the first half of this year, specifically Provenge, which has a cost of $93,000 for three infusions. Vpriv costs $170,000 or approximately 15% less than Genzyme's Cerezyme, which costs approximately $200,000 per year of therapy. Because demand exceeds supply for Gaucher disease, formulary positioning has not yet occurred. Other new entries have had relatively little uptake to date. *See Figure 52, 2010 FDA-Approved Injectable Drugs/Indications – Specialty and Oncology.*

Two key biosimilar therapies are currently in the pipeline: ESA and granulocyte colony-stimulating factor (G-CSF) products. Teva's Neutroval is closest to market entry; however, FDA delayed approval on September 30, 2010. *See Figure 53, Biosimilar Pipeline.*

Non-small cell lung and breast cancers have the most robust pipelines, with nearly 90 agents in phase 2 and 3 study for each. Colorectal, prostate, melanoma, ovarian, and non-Hodgkin's lymphoma have between 30 and 40 drugs under study for each cancer type. *See Figure 54, Pipeline Drugs in Various Phases of Study for Key Cancer Types, and Figure 55, Selected Phase 3 Products by Key Cancer Type.*

FIG. 52 2010 FDA-APPROVED INJECTABLE DRUGS

DRUG	MANUFACTURER	INDICATION	APPROVAL
Actemra (tocilizumab)	Genentech	Rheumatoid Arthritis	January
Vpriv (velaglucerase alfa)	Shire	Type 1 Gaucher Disease	March
Provenge (sipuleucel-T)	Dendreon	Prostate Cancer	May
Prolia (denosumab)	Amgen	Osteoporosis	June
Jevtana (cabazitaxel)	Sanofi Aventis	Prostate Cancer	June
Krystexxa (pegloticase)	Savient Pharmaceuticals	Chronic Gout (hyperuricemia)	September
Herceptin (trastuzumab)	Genentech	Gastric Cancer	October
Xgeva (denosumab)	Amgen	Bone Metastases	November
Halaven (eribulin mesylate)	Eisai	Breast Cancer	November

Source: FDA-approved drugs. CenterWatch website. http://www.centerwatch.com/drug-information/fda-approvals. Accessed November 24, 2010.

FIG. 53 BIOSIMILAR PIPELINE

PRODUCT NAME/CLASS	PROPOSED INDICATION	COMPANY	PHASE OF FDA STUDY	COMMENTS
XM02 (Neutroval)	Reduction in the duration of severe neutropenia and the incidence of febrile neutropenia in patients treated with established myelosuppressive chemotherapy for cancer	Teva	N/A	Follow-on biologic for Neupogen. The FDA has accepted Teva's biologics license application for XM02.
MK-2578 (pegylated erythropoietin)	Anemia, chronic kidney disease	Merck	Ongoing phase 2 study	Follow-on biologic for Procrit; estimated launch 2012.
INS-19 (investigational recombinant granulocyte colony-stimulating factor)	Treatment of neutropenia in patients receiving chemotherapy or bone marrow transplants, or who have clinically low neutrophils for other reasons	Merck/INSMED	Ongoing phase 1 study	Follow-on biologic for Neupogen. Merck purchased INSMED's portfolio of follow-on biologics in Feb. 2009.
INS-20 (pegylated recombinant granulocyte colony-stimulating factor)	Treatment of neutropenia in patients receiving chemotherapy or bone marrow transplants, or who have clinically low neutrophils for other reasons	Merck/INSMED	Ongoing phase 1 study	Follow-on biologic for Neulasta. Merck purchased INSMED's portfolio of follow-on biologics in Feb. 2009.

FIG. 54 | PIPELINE DRUGS IN VARIOUS PHASES OF STUDY FOR KEY CANCER TYPES

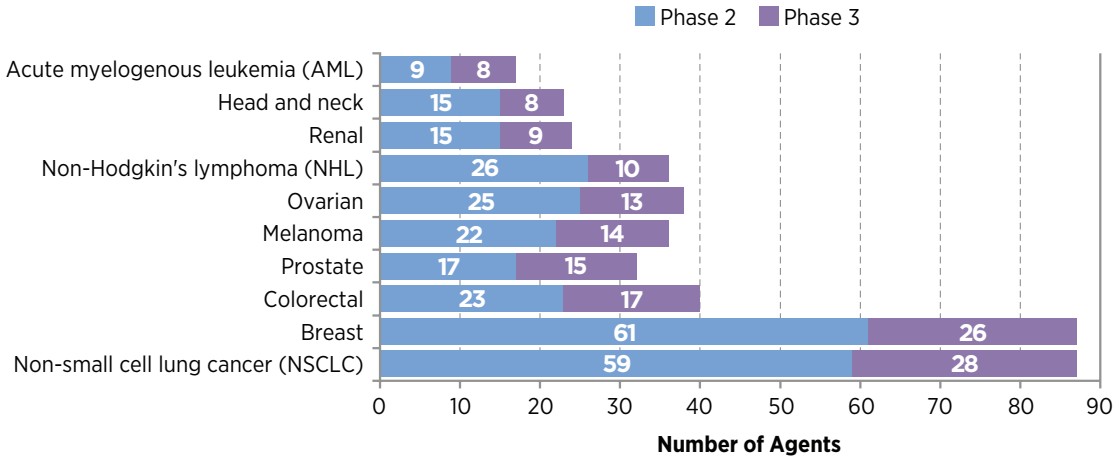


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FIG. 55 | SELECTED PHASE 3 PRODUCTS BY KEY CANCER TYPE

NON-SMALL CELL LUNG CANCER (NSCLC)		
PRODUCT NAME	**CLASS**	**AREA(S) OF STUDY**
Abraxane; nab-paclitaxel	microtubule inhibitor	first-line metastatic
aflibercept; vascular endothelial growth factor (VEGF) trap	VEGF-A inhibitor	second-line metastatic
Avastin; bevacizumab	anti-VEGF monoclonal antibody	adjuvant; NSCLC with previously treated central nervous system metastases
crizotinib; PF-02341066	ALK inhibitor (oral)	adjuvant
Erbitux; cetuximab	anti-epidermal growth factor receptor (EGFR) monoclonal antibody	NSCLC
iniparib; BSI-201	poly (ADP-ribose) polymerase (PARP) inhibitor	squamous cell lung cancer
Iressa; gefitinib	EGFR tyrosine kinase inhibitor	NSCLC
Lucanix; belagenpumatucel-L	immunotherapy	NSCLC
motesanib diphosphate; AMG 706	anti-VEGF receptors 1, 2, and 3 (VEGFR 1-3) (oral)	first-line metastatic
necitumumab; IMC-11F8	EGFR inhibitor	NSCLC
Nexavar; sorafenib	multiple tyrosine kinase inhibitor	first-line metastatic
Opaxio; paclitaxel poliglumex; CT-2103	microtubule inhibitor	NSCLC
PF-00299804	pan-HER inhibitor	metastatic
Stimuvax; BLP25 liposome vaccine	immunotherapy	NSCLC
Sutent; sunitinib malate	multiple tyrosine kinase inhibitor	NSCLC
talactoferrin	dendritic cell activator (DCA)	locally advanced or metastatic
Tarceva; erlotinib	HER1/EGFR inhibitor	adjuvant
Tovok; afatinib; BIBW 2992	EGFR/HER2 inhibitor	NSCLC
vadimezan; ASA404 (DMXAA)	vascular disrupting agent	second-line metastatic
Vargatef; BIBF 1120	multiple tyrosine kinase inhibitor (VEGFR; fibroblast growth factor receptor, FGFR; platelet-derived growth factor receptor, PDGFR)	NSCLC

BREAST		
PRODUCT NAME	CLASS	AREA(S) OF STUDY
Aromasin; exemestane	aromatase inhibitor	breast cancer
arzoxifene	selective estrogen receptor modulator (SERM)	breast cancer
Avastin; bevacizumab	anti-VEGF monoclonal antibody	first-line metastatic (HER2-) and (HER2+); second-line metastatic; adjuvant (HER2-) and (HER2+)
Doxil; doxorubicin hydrochloride	anthracycline antibiotic	metastatic
Faslodex; fulvestrant	oestrogen receptor antagonist	first-line metastatic
Herceptin; trastuzumab	antibody drug conjugate	adjuvant (HER2+)
iniparib; BSI-201	PARP inhibitor	metastatic (triple negative)
Ixempra; ixabepilone	epothilone	adjuvant
neratinib; HKI-272	ErbB1 and ErbB2 inhibitor	advanced (HER2+)
NeuVax; NeuVax (E75)	immunotherapy (peptide-based)	adjuvant (HER2+)
Omnitarg; pertuzumab; R1273	HER dimerization inhibitor	first-line metastatic (HER2+)
ramucirumab; IMC-1121B	anti-VEGFR-2 monoclonal antibody	metastatic
Stimuvax; BLP25 liposome vaccine	immunotherapy	second-line metastatic
Tavocept; dimensa; BNP7787	chemoprotective agent	metastatic
trastuzumab-DM1	antibody drug conjugate	second-line metastatic (HER2+)
Tykerb; lapatinib	ErbB2 and EGFR dual kinase inhibitor	first-line metastatic; adjuvant
Votrient (+ Tykerb); pazopanib (+ lapatinib)	multiple tyrosine kinase inhibitor	inflammatory
Xeloda; capecitabine	fluoropyrimidine (oral)	adjuvant
Zometa; zoledronic acid	bisphosphonate	breast cancer

COLORECTAL		
PRODUCT NAME	CLASS	AREA(S) OF STUDY
aflibercept; VEGF trap	VEGF-A inhibitor	second-line metastatic
Aptocine	light-activated drug treatment	metastatic
axitinib; AG013736	multiple tyrosine kinase inhibitor (VEGFR-1, 2, 3, PDGFR, cKIT)	second-line metastatic
brivanib	VEGFR-2 inhibitor	metastatic
Erbitux; cetuximab	anti-EGFR monoclonal antibody	first-line metastatic; adjuvant
Recentin; cediranib	multiple tyrosine kinase inhibitor (VEGF 1, 2, 3)	colorectal cancer
S-1	fluoropyrimidine (oral)	colorectal cancer
Tarceva; erlotinib	HER1/EGFR inhibitor	colorectal cancer
Vectibix; panitumumab	anti-EGFR monoclonal antibody (humanized)	first-line metastatic; second-line metastatic
Xeloda; capecitabine	fluoropyrimidine (oral)	first-line metastatic; second-line metastatic; adjuvant
Xeloda; capecitabine	fluoropyrimidine (oral)	second-line metastatic

PROSTATE		
PRODUCT NAME	**CLASS**	**AREA(S) OF STUDY**
abiraterone; CB-7630	inhibitor of the steroidal enzyme 17 alpha-hydroxylase/C17,20 lyase (oral)	first-line hormone refractory
aflibercept; VEGF trap	VEGF-A inhibitor	first-line hormone refractory
Alpharadin; radium-223 chloride	alpha-emitting radiopharmaceutical	treatment of bone metastases in hormone refractory prostate cancer
Avastin; bevacizumab	anti-VEGF monoclonal antibody	hormone refractory
cabazitaxel; XRP6258	taxane	first-line hormone refractory
DCVax	immunotherapy	prostate cancer
Fareston; toremifene	SERM	prevention of bone fractures; prevention of prostate cancer in men with high-grade prostatic intraepithelial neoplasia
MDV3100	selective androgen receptor modulator (SARM)	hormone refractory
OGX-011/TV-1011 (+ docetaxel)	clusterin inhibitor	second-line metastatic hormone refractory
phenoxodiol	multiple signal transduction regulator	prostate cancer
satraplatin	platinum chemotherapy agent (oral)	second-line metastatic hormone refractory (docetaxel refractory)
Sutent; sunitinib malate	multiple tyrosine kinase inhibitor	hormone refractory
zibotentan; ZD4054	endothelin A receptor antagonist	hormone refractory

MELANOMA		
PRODUCT NAME	**CLASS**	**AREA(S) OF STUDY**
Abraxane; nab-paclitaxel	microtubule inhibitor	first-line metastatic
Allovectin-7	immunotherapy	first-line metastatic
Genasense; oblimersen sodium	Bcl-2 inhibitor	metastatic
ipilimumab; MDX-010	anti-CTLA4 monoclonal antibody (humanized)	first-line metastatic; second-line metastatic; adjuvant
Nexavar; sorafenib	multiple tyrosine kinase inhibitor	melanoma
Oncophage; vitespen	immunotherapy	metastatic
OncoVEX granulocyte-macrophage colony-stimulating factor	modified herpes-simplex 1 virus injected directly into tumor	metastatic
Pegintron; peginterferon alfa-2b	PEG recombinant alpha-2b interferon	melanoma
PLX4032 (RG7204)	BRAF-selective kinase inhibitor	melanoma
The Delcath system	drug delivery platform	metastatic in the liver
Zadaxin; thymalfasin	immune system modulator	melanoma

OVARIAN		
PRODUCT NAME	CLASS	AREA(S) OF STUDY
alkeran	alkylating agent	ovarian cancer
AMG 386 (+ paclitaxel)	Fc-peptide fusion protein targeting angiopoietins (peptibody)	second-line metastatic
Avastin; bevacizumab	anti-VEGF monoclonal antibody	first-line metastatic; second-line metastatic platinum-sensitive
farletuzumab; MORAb-003	IgG1 monoclonal antibody (humanized)	second-line metastatic
Hycamtin; topotecan hydrochloride	topoisomerase inhibitor	first-line metastatic
Karenitecin; karenitecin; BNP1350	highly lipophilic camptothecin	ovarian cancer
Opaxio; paclitaxel poliglumex; CT-2103	microtubule inhibitor	ovarian cancer
patupilone; EPO906	epothilone	ovarian cancer
phenoxodiol	multiple signal transduction regulator	ovarian cancer
Tarceva; erlotinib	HER1/EGFR inhibitor	ovarian cancer
Vargatef; BIBF 1120	multiple tyrosine kinase inhibitor (VEGFR, FGFR, PDGFR)	ovarian cancer

NON-HODGKIN'S LYMPHOMA (NHL)		
PRODUCT NAME	CLASS	AREA(S) OF STUDY
Arzerra; ofatumumab	anti-CD20 monoclonal antibody (humanized)	second-line follicular
Avastin; bevacizumab	anti-VEGF monoclonal antibody	diffuse large B-cell lymphoma (DLBCL)
BiovaxID	immunotherapy	follicular
enzastaurin	serine/threonine kinase inhibitor	DLBCL
galiximab	anti-CD80 monoclonal antibody	B-cell
pixantrone; BBR 2778	anthracycline	second-line diffuse large B-cell
Rituxan; rituximab	anti-CD20 monoclonal antibody	first-line follicular
Velcade; bortezomib	proteasome inhibitor	second-line follicular

RENAL		
PRODUCT NAME	CLASS	AREA(S) OF STUDY
axitinib; AG013736	multiple tyrosine kinase inhibitor (VEGFR-1, 2, 3; PDGFR; cKIT)	second-line metastatic
Nexavar; sorafenib	multiple tyrosine kinase inhibitor	adjuvant
Oncophage; vitespen	immunotherapy	metastatic
Sutent; sunitinib malate	multiple tyrosine kinase inhibitor	first-line metastatic; adjuvant; cytokine-refractory metastatic
tivozanib; AV-951	VEGF receptors 1, 2, and 3 inhibitor	first-line metastatic
Torisel; temsirolimus	mTOR inhibitor	renal cell carcinoma

HEAD AND NECK		
PRODUCT NAME	**CLASS**	**AREA(S) OF STUDY**
Alimta; pemetrexed (+ cisplatin)	antimetabolite (a folic acid antagonist)	recurrent or metastatic (squamous)
Avastin; bevacizumab	anti-VEGF monoclonal antibody	metastatic
Multikine	immunotherapy	first-line
OncoVEX GM-CSF	modified herpes-simplex 1 virus injected directly into tumor	first-line
Selective Electrochemical Tumor Ablation (SECTA) + (bleomycin)	electroporation therapy	head and neck cancer
Vectibix; panitumumab	anti-EGFR monoclonal antibody (humanized)	metastatic; recurrent
zalutumumab (+ radiotherapy); HuMax-EGFr	anti-EGFR monoclonal antibody (humanized)	first-line

ACUTE MYELOGENOUS LEUKEMIA (AML)		
PRODUCT NAME	**CLASS**	**AREA(S) OF STUDY**
amonafide malate; AS1413	topoisomerase inhibitor	AML
Ceplene; histamine dihydrochloride	histamine H2 receptor agonist	AML
Clolar; clofarabine	antimetabolite	AML
midostaurine; PKC412	multiple tyrosine kinase inhibitor	AML
Onrigin; laromustine	alkylating agent	AML
sapacitabine; CYC682	antimetabolite (oral)	AML
Trisenox; arsenic trioxide	taxane (a synthetic retinoid)	AML
vosaroxin; SNS-595	topoisomerase 2 inhibitor	AML

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Key Legislative Outcomes – 2010[8]

The Patient Protection and Affordable Care Act (PPACA) provisions affecting prescription drug coverage include:

- Coverage expansion: Provides for a significant expansion of coverage to the uninsured through a Medicaid expansion, an individual requirement to obtain health insurance, and subsidies to help low- and middle-income individuals buy coverage through newly established health benefit exchanges.
- PPACA provides that prescription drugs are one of the "essential health benefits" that must be included in health plans in the exchanges and in the benchmark benefit package or benchmark equivalent for newly eligible adults under Medicaid.
  - Medicare changes provide for the following:
    - A $250 rebate to Medicare Part D beneficiaries with out-of-pocket spending in the Medicare Part D coverage gap in 2010
    - A 50% discount for brand-name drugs for beneficiaries in the coverage gap starting in 2011
    - A phasing in of coverage in the gap for generic and brand-name drugs that will reduce the beneficiary coinsurance rate from 100% in 2010 to 25% in 2020
    - A reduction between 2014 and 2019 in the threshold that qualifies enrollees for catastrophic coverage
    - An elimination of the tax deduction for employers who receive Medicare Part D retiree drug subsidy payments, starting in 2013

In the coming years, implementation of various provisions of PPACA will affect prescription drug coverage, utilization, prices, and regulation. Coverage and utilization of prescription drugs will be expanded by: PPACA's health insurance mandate and premium and cost-sharing subsidies; the designation of prescription drugs as an essential health benefit to be covered by private health plans through the new health benefit exchanges and by Medicaid for newly eligible adults; and Medicare's prescription drug rebate, cost-sharing, and catastrophic threshold changes. Prices charged to government programs will be affected by changes to Medicaid rebate requirements and expansions to the Section 340B program. Prescription drug regulation will be affected by the new process for licensure of biosimilar versions of brand-name biological products and by drug-labeling requirements. These and other PPACA changes will ultimately impact national spending for prescription drugs in ways yet to be seen.

[8] Kaiser Family Foundation

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A Benchmark for Medical Injectables

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