Trends in Medicaid Reimbursements for Insulin From 1991 Through 2014

Jing Luo, MD; Jerry Avorn, MD; Aaron S. Kesselheim, MD, JD, MPH

IMPORTANCE Insulin is a vital medicine for patients with diabetes mellitus. Newer, more expensive insulin products and the lack of generic insulins in the United States have increased costs for patients and insurers.

OBJECTIVE To examine Medicaid payment trends for insulin products. Cost information is available for all 50 states and has been recorded since the 1990s.

DESIGN, SETTING, AND PARTICIPANTS A time-series analysis comparing reimbursements and prices. Using state- and national-level Medicaid data from 1991 to 2014, we identified all patients who used 1 or more of the 16 insulin products that were continuously available in the United States between 2006 and 2014. Insulin products were classified into rapid-acting and long-acting analogs, short-acting, intermediate, and premixed insulins based on American Diabetes Association Guidelines.

MAIN OUTCOMES AND MEASURES Inflation-adjusted payments made to pharmacies by Medicaid per 1 mL (100 IU) of insulin in 2014 US dollars.

RESULTS Since 1991, Medicaid reimbursement per unit (1 mL) of insulin dispensed has risen steadily. In the 1990s, Medicaid reimbursed pharmacies between $2.36 and $4.43 per unit. By 2014, reimbursement for short-acting insulins increased to $9.64 per unit; intermediate, $9.22; premixed, $14.79; and long-acting, $19.78. Medicaid reimbursement for rapid-acting insulin analogs rose to $19.81 per unit. The rate of increase in reimbursement was higher for insulins with patent protection ($0.20 per quarter) than without ($0.05 per quarter) ($P < .001$). Total Medicaid reimbursements peaked at $407.4 million dollars in quarter 2 of 2014. Total volume peaked at 29.9 million units in quarter 4 of 2005 and was 21.2 million units in quarter 2 of 2014.

CONCLUSIONS AND RELEVANCE Between 1991 and 2014, there was a near-exponential upward trend in Medicaid payments on a per-unit basis for a wide variety of insulin products regardless of formulation, duration of action, and whether the product was patented. Although reimbursements for newer, patent-protected insulin analogs increased at a faster rate than reimbursements for older insulins, payments increased for all products we examined. Our findings suggest a lack of price competition in the United States for this class of medications.
Insulin was isolated in the late 1800s and first injected into a patient with diabetes mellitus in 1922.\textsuperscript{1,2} Banting, Best, and Collip licensed their patent for the process of isolating insulin for 1 dollar each as a gift to humanity rather than an opportunity for commercial profit.\textsuperscript{3} The earliest commercial insulin preparations lacked purity and varied in potency.\textsuperscript{4} Manufacturing improvements over the past 90 years have resulted in safer and more convenient forms of insulin for patients with diabetes mellitus.\textsuperscript{5,6}

However, improvements in insulin formulations have come with increased costs.\textsuperscript{6-11} In recent years, studies have demonstrated a shift in use from older forms of insulin (eg, human insulin) to newer, more expensive analogs.\textsuperscript{6-12} A recent article traced the historical evolution of insulin from animal to human to synthetic analogs.\textsuperscript{9} Although the comparative evidence of clinical benefit for newer insulins is limited, with a few studies suggesting reduced rates of nocturnal hypoglycemia or improved adherence,\textsuperscript{13-15} newer analogs are generally more expensive than older insulin formulations.\textsuperscript{12} These changes in the insulin market contributed to an increase in out-of-pocket expenditures for those with private health insurance.\textsuperscript{16} High costs also strain the budgets of government payors such as Medicaid.\textsuperscript{16,17}

One contributor to the high cost of insulin is the lack of competition. Currently, 3 manufacturers (Eli Lilly, Sanofi Aventis, and Novo Nordisk) account for more than 90% of the global insulin market.\textsuperscript{18,19} They also produce the entire insulin supply for approximately 3 million adult diabetic patients in the United States.\textsuperscript{20} For these reasons, the US insulin market behaves differently from the trend in pharmaceutical markets where generic competition results in substantial price reductions after patent expiration.\textsuperscript{21} Although generic insulins may become available to patients in the United States in the next several years (glargine [Abasaglar; Lilly/Boehringer Ingelheim] has been available in Europe since September 2014), there are currently no generic manufacturers that produce insulin for the US market.

We examined trends in Medicaid payments for currently available insulin products in the United States from 1991 to 2014. We chose Medicaid because cost information is available for all 50 states and the District of Columbia and has been recorded consistently since the start of the Medicaid Drug Rebate Program in 1990. Additionally, Medicaid programs are sensitive to changes in costs and cover a high-risk patient population with little capacity to absorb additional costs of medications themselves.

Methods

Using the US Food and Drug Administration’s (FDA) National Drug Code (NDC) Directory, we obtained a list of all commercial insulin products marketed to patients in the United States in December 2014. We used the Drug Topics Red Book to identify a subsample of insulin products that were both recently available and continuously marketed and then cross-referenced this list with what was available in 2006 when the Medicare Part D prescription drug benefit that also affected the number of patients receiving pharmacy benefits from Medicaid was started.\textsuperscript{22} We excluded NDCs from discontinued products and repackagers. We also excluded regular human insulin, U-500 (concentrated) (Humulin R U-500; Eli Lilly and Company) due to its atypical dosage strength. Humulin R U-500 is different from all other insulin products because it contains 500 IU per 1 mL of solution; other insulin products typically contain 100 IU per 1 mL. The remaining 16 products were classified into rapid-acting and long-acting analogs, short-acting, intermediate, and premixed insulins based on American Diabetes Association Guidelines (Table 1).

We obtained quarterly data on reimbursements and the number of units procured for each of these insulin products from the Medicaid State Drug Utilization Database. We excluded data from the third quarter of 2001 to the fourth quarter of 2002 for aspart (Novolog; Novo Nordisk) vials in Minnesota and excluded the first quarter of 2012 to the second quarter of 2012 for NPH (Novolin N; Novo Nordisk) vials in Hawaii because they were extreme outliers. In these cases, the amount reimbursed per unit was approximately 20-fold higher than the national mean. We aggregated the remaining state-level data to form national totals and examined data from the first quarter of 1991 to the second quarter of 2014. We standardized payments per NDC unit by dividing total Medicaid reimbursements in US dollars by the total number of units procured for each quarter. To account for different formulations, we report reimbursements per NDC unit, with each unit representing 1 mL (100 IU) of standard-strength insulin.

We adjusted for inflation using annual Consumer Price Indexes and report all values in 2014 US dollars. For the primary time-series analysis, we plotted reimbursements per NDC unit of insulin against calendar time in quarters. We used the line chart option in Excel 2007 (Microsoft Corporation) to generate cost figures. This charting option is a standard way of summarizing data recorded over time and connects plotted values using simple lines. No curve fitting or regression techniques were used. Total reimbursements include dispensing fees but exclude manufacturer rebates or rebates from supplemental rebate agreements, which are confidential agreements between drug manufacturers and states that allow additional rebates beyond what is mandated by the Centers for Medicare and Medicaid Services.

To place insulin costs in a clinical context, we compared average quarterly Medicaid reimbursements for a typical patient with diabetes and assumed daily use of 40 IU of insulin per day (0.4 NDC units) based on the standard established by the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system guidelines for the defined daily dose of basal insulin.\textsuperscript{24} Assuming use of only 1 insulin product at a time and no wasted insulin, the typical diabetic in our study would require 14 400 IU (40 IU/d × 30 d/mo × 12 mo/y) of insulin per year. We report annual costs to Medicaid at 3 time points: 1991 (start of database), 2001 (market introduction of glargine), and 2014 (end of database). We chose 2001 as a relevant time point because it represented 10 years after the start of our study period, and it marked the year of introduction of glargine (Lantus; Sanofi-Aventis), the top-selling insulin prod-
uct in the United States. In 2014, there were more than 19.7 million prescriptions for this long-acting insulin analog.\textsuperscript{25}

To compare rate of increase in reimbursements of patented with nonpatent-protected insulins, we used generalized linear models (PROC GLM) and an interaction term between year and patent status. A product was considered patented if there was a nonexpired patent in the FDA list of approved drug products with therapeutic equivalence evaluations (Orange Book) as of January 2013.\textsuperscript{23} All computing was performed using SAS 9.4 (SAS Institute) or Excel 2007 (Microsoft Corporation).

### Results

Since 1991, quarterly Medicaid reimbursements for insulin products on a per-unit basis have steadily increased (Figure 1). In the 1990s, Medicaid reimbursed pharmacies between $2.36 and $4.43 per NDC unit (1 mL) of insulin. By 2014, this figure increased to $9.64 per unit for short-acting and $9.24 per unit for intermediate insulins. For premixed insulins, the rate in 2014 was $14.79 per unit.

### Table 1. Insulin Products Continuously Available in the United States Since 2006

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Brand Name(^b)</th>
<th>Generic Name</th>
<th>Covered by Active Patent(^c)</th>
<th>NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-acting</td>
<td>Humalog vials</td>
<td>Lispro</td>
<td>Yes</td>
<td>0002751001</td>
</tr>
<tr>
<td></td>
<td>Humalog Kwikpen</td>
<td>Lispro</td>
<td>Yes</td>
<td>0002879959</td>
</tr>
<tr>
<td></td>
<td>Novolog vials</td>
<td>Aspart</td>
<td>Yes</td>
<td>0169750111</td>
</tr>
<tr>
<td></td>
<td>Novolog Flexpen</td>
<td>Aspart</td>
<td>Yes</td>
<td>0169633910</td>
</tr>
<tr>
<td></td>
<td>Novolog Penfill Cartridge</td>
<td>Aspart</td>
<td>Yes</td>
<td>0169330312</td>
</tr>
<tr>
<td></td>
<td>Apidra vials</td>
<td>Glulisine</td>
<td>Yes</td>
<td>0088250033</td>
</tr>
<tr>
<td>Long-acting</td>
<td>Lantus vials</td>
<td>Gargin</td>
<td>Yes</td>
<td>0088220033</td>
</tr>
<tr>
<td></td>
<td>Levemir vials</td>
<td>Detemir</td>
<td>Yes</td>
<td>0169368712</td>
</tr>
<tr>
<td>Premixed</td>
<td>Novolog Mix 70/30 vials</td>
<td>70% Aspart protamine/30% aspart</td>
<td>Yes</td>
<td>0169368512</td>
</tr>
<tr>
<td></td>
<td>Novolog Mix 70/30 Flexpen</td>
<td>70% Aspart protamine/30% aspart</td>
<td>Yes</td>
<td>0169369619</td>
</tr>
<tr>
<td></td>
<td>Humulin 70/30 vials</td>
<td>70% Isophane/30% regular [rDNA origin]</td>
<td>No</td>
<td>0002871501</td>
</tr>
<tr>
<td></td>
<td>Novolin 70/30 vials</td>
<td>70% Isophane/30% regular [rDNA origin]</td>
<td>No</td>
<td>0169183711</td>
</tr>
<tr>
<td>Short-acting</td>
<td>Humulin R vials</td>
<td>Regular</td>
<td>No</td>
<td>0002821501</td>
</tr>
<tr>
<td></td>
<td>Novolin R vials</td>
<td>Regular</td>
<td>No</td>
<td>0169183311</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Novolin N vials</td>
<td>NPH (isophane)</td>
<td>No</td>
<td>0169183411</td>
</tr>
<tr>
<td></td>
<td>Humulin N vials</td>
<td>NPH (isophane)</td>
<td>No</td>
<td>0002831501</td>
</tr>
</tbody>
</table>

Abbreviations: FDA, US Food and Drug Administration; NDC, National Drug Code.

\(^a\) Discontinued products are not included.

\(^b\) The manufacturers of the brand name insulins listed are Eli Lilly and Company (Humalog vials, Humalog Kwikpen, Humulin 70/30 vials, Humulin R vials, Humulin N vials), Novo Nordisk (Novolog vials, Novolog Flexpen, Novolog Penfill Cartridge, Levemir vials, Novolog Mix 70/30 vials, Novolog Mix 70/30 Flexpen, Novolin 70/30 vials, Novolin 70/30, Novolin R vials, Novolin N vials), and Sanofi-Aventis (Apidra vials, Lantus vials).

\(^c\) According to patent expiration dates found in the FDA Orange Book\textsuperscript{23} as of January 2013.

Figure 1. Medicaid Reimbursement Trends for Covered Insulin Products From 1991 Through 2014

Reimbursements were adjusted by the Bureau of Labor Statistics’ annual Consumer Price Index for All Urban Consumers.
Medicaid reimbursements for rapid-acting insulin analogs have increased from $3.69 per unit when this class of insulins first appeared on the US market to $19.81 per unit in 2014. Long-acting insulins have historically been reimbursed at lower rates than rapid-acting analogs; however, a steep rise in payments during 2012 to 2014 for long-acting insulins has resulted in near-parity in reimbursements between these 2 categories ($19.78 for long-acting insulins vs $19.81 for rapid-acting analogs in the second quarter of 2014). The rate of increase of reimbursements was higher for patented insulin products (ie, insulin analogs) than for nonpatent-protected insulins (ie, human insulin) (P < .001, Figure 2). When glargine was first introduced in 2001, patent-protected insulins were reimbursed on average at a rate that was 76% higher than the rate for nonpatent-protected insulins. By 2014, this rate had increased to 111%.

Total reimbursements by Medicaid for insulin increased from $10.7 million in the first quarter of 1991 to $178.5 million in the fourth quarter of 2005. After the start of Medicare Part D in January 2006, millions of patients had their coverage of insulin prescriptions switched from Medicaid to Medicare. As a result, Medicaid reimbursements for insulin fell to $88 million for the first quarter of 2006. However, insulin reimbursements rose quickly and surpassed the previous 2005 high by the fourth quarter of 2010 ($191.3 million). Since 2010, quarterly reimbursements have risen sharply, with record highs every quarter until the second quarter of 2014 ($407.4 million).

Volume for insulin products rose in a manner similar to reimbursements: from 3.9 million units in the first quarter of 1991 to a peak of 29.9 million units (approximately 3 million vials) in 2005. After the start of Medicare Part D, the volume of insulin purchased by Medicaid dropped in the first quarter of 2006 to 14.6 million units. As of the second quarter of 2014, Medicaid procured 21.2 million units of insulin.

For a patient with diabetes mellitus requiring 40 U of insulin per day, the annual inflation-adjusted cost to Medicaid for medication and dispensing fees was $370 for an average priced premixed insulin in 1991 and $2852 for an average priced rapid-acting insulin in 2014 (Table 2). Since the introduction of glargine in 2001, the annual cost to Medicaid for the same insulin products has increased from 284% for intermediate-acting to 455% for premixed insulins.

When insulin pens were compared with insulin vials for the 16 insulin products in our study, the change in Medicaid reimbursements did not substantially differ (data not shown).

Table 2. Estimated Annual Medicaid Payments for Insulin for a Patient Requiring 40 Units per Day

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Cost at Quarter 2, $*</th>
<th>Change, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-acting</td>
<td>771</td>
<td>2852</td>
</tr>
<tr>
<td>Long-acting</td>
<td>891</td>
<td>2848</td>
</tr>
<tr>
<td>Premixed</td>
<td>370</td>
<td>468</td>
</tr>
<tr>
<td>Short-acting</td>
<td>399</td>
<td>481</td>
</tr>
<tr>
<td>Intermediate</td>
<td>383</td>
<td>468</td>
</tr>
</tbody>
</table>

Discussion

Between 1991 and 2014, we found a near-exponential upward trend in Medicaid payments for a wide variety of insulin products regardless of formulation, duration of action, and whether or not the product was patented. Although reimbursements for newer insulin analogs that are protected by patent are increasing at a faster rate than reimbursements for older insulins, quarterly payments increased for all products we examined.

The choice of which insulin to start is clinical and based on a variety of factors. Some patients may require both basal and mealtime insulins to achieve adequate glycemic control. Other patients may prefer the convenience of prefilled pens or longer-duration analogs regardless of cost. As overall costs rise, state Medicaid programs are likely to increasingly use prescription management strategies to reduce drug spending. Such measures will disproportionately affect newer, more expensive insulin analogs. Medicaid prescription management strategies may reduce therapeutic alternatives for patients and make it more difficult for physicians to prescribe certain regimens.

From a policy perspective, our findings suggest that the insulin market in the United States lacks price competition. Some degree of competition might be expected owing to the diversity of insulin formulations available and the fact that 3 manufacturers control the market rather than just 1. The lack of insulin price competition follows a traditional pattern in the United States when a market for a particular drug product is controlled by a small number of brand-name manufacturers. For example, after the approval of brand-name omeprazole (Prilosec; AstraZeneca) in 1989, introduction of other brand-name proton-pump inhibitors (eg, lansoprazole [Prevacid; Takeda], 1995; rabeprazole [Aciphex; Eisai], 1999; pantoprazole [Protonix; Pfizer], 2000; and esomeprazole [Nexium; AstraZeneca], 2001) did not lead to lower prices among those brand-name drugs.

It is to be expected that the price of brand-name drugs will increase over time. A study by the US Government Accountability Office found that between the first quarter of 2006 and the first quarter of 2010, retail prices obtained from Pennsylvania's Pharmaceutical Assistance Contract for the Elderly program for a basket of 55 brand name and 45 generic prescription drugs (including only 1 insulin product: glargine) increased at an average annual rate of 6.6% (unadjusted for inflation). By contrast, our time-series analyses show that during this same time period, Medicaid reimbursement per unit of insulin increased by 10.1% per year (unadjusted) and 7.9% per year (adjusted by Consumer Price Indexes [CPI]).

Prior research has suggested that costs associated with insulin treatment are increasing because of the widespread adoption of insulin therapy and increasing use of newer, more expensive insulin analogs. Others have suggested that rising insulin costs are related to incremental innovation by brand-name manufacturers that has repeatedly precluded the development of a generic insulin industry in the United States. In this period, many manufacturers introduced insulin analogs that were similar to the market leader, creating barriers to market entry for generics and thereby allowing manufacturers to influence the development of a generic insulin industry in the United States. Insulin manufacturers may be introducing gradual innovation in insulin formulations and delivery devices as a way to protect and extend their products’ patent life, a practice called life cycle management or evergreening. As some of these newer products age and approach the loss of their patent protection (or when a competing patented product enters the market), manufacturers may increase prices as a way to offset future revenue losses. Although some price increases may be warranted, such as when a new product provides clear benefits, the prices of older insulin formulations should drop or stay the same over time. Our analysis shows, however, that this result has not been the case. Even after adjusting for inflation, prices and reimbursements for all insulin products have been increasing on a per-unit basis, regardless of their degree of innovation.

A limitation of our study was that we could not determine net costs to states because manufacturer drug rebate amounts are confidential, as are state supplemental rebate agreements. It is unlikely, however, that rebates would offset the increases in payments that we identified because base Medicaid rebates for innovator drugs are the greater of 23.1% of the average manufacturer price (AMP) or the difference between AMP and the best price (the lowest price offered to any purchaser of that product, with a few exceptions, such as for drugs purchased by the Department of Veterans Affairs). Another limitation was that we did not have data on state-by-state variation in prescription management strategies for insulin products (eg, formulary tier and cost-sharing) which can affect prescribing patterns, costs, and patient adherence. Finally, our sample did not include reimbursement data from discontinued insulins or from any insulin products first marketed in the United States after 2006.

Numerous policy options can be employed to combat rising insulin prices. If manufacturer rebates to Medicaid and other publicly funded insurance programs were transparent, net spending on these products would be known, which could help buyers negotiate more favorable purchasing contracts. Additionally, pricing standardization could decrease any state-to-state variability for medication purchases. Currently, there is wide variation in the formulas that states use to calculate reimbursements for drug ingredient costs. Despite efforts to establish a single national pricing benchmark based on actual drug acquisition costs, many states continue to calculate ingredient costs based on published average wholesale prices or wholesale acquisition costs. These methods are not ideal because they reflect manufacturer suggested list prices rather than actual drug costs.

In addition, the FDA should clarify the steps needed to bring a generic version of insulin to the market, similar to the case in Europe. An application for a formulation of glargine (Abasaglar; Eli Lilly and Boehringer Ingelheim) has been approved in Europe, but it remains unavailable in the United States owing partially to ongoing litigation. Thus for the foreseeable future, insulin prices may continue to increase, notwithstanding that 6 of the 16 insulin products we studied have been off patent for many years and another 3 should soon be off patent (aspart, lispro, and glargine). By contrast, FDA analyses show that generic drug prices reach about 55% of the brand-name price when 2 competitors are in the market, 33% when
there are 5 generic competitors, and 13% when there are 15. 37
To expedite generic entry in this field, the FDA should
consider not requiring a new full set of clinical efficacy data if the
proposed generic insulin can be proven to have similar physi-
cal and chemical properties to the reference product in vitro
and preclinical studies.

Generic entry alone may not be sufficient to control the
costs of insulin products. Potential competitors may be dis-
couraged to enter the market by the high costs associated
with manufacturing, storing, and distributing insulin. Other fac-
tors such as interchangeability, state pharmacy substitution
laws, and market dynamics may ultimately determine the de-
gree of competition and cost savings. 38 For example, even if
generic glargine enters the market within the next few years,
it would still need to compete against Sanofi’s authorized ge-
neric formulation for glargine (a brand-name drug product
sold as a generic by a licensee or subsidiary), as well as the Lan-
tus Solostar (Sanofi-Aventis) pen-type injector (not included
in our analysis) with a device patent lasting until September
2024.

Conclusions
We found that reimbursements for many commonly used ins-
ulin products have been increasing at a dramatic rate. If these
trends continue without price controls from robust generic
competition, patients, physicians, and public and private in-
surers will find it increasingly difficult to pay for this special-
ized class of essential medicines.

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Avorn, Kesselheim.
Drafting of the manuscript: Luo.
Critical revision of the manuscript for important intel-
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Correction: This article was corrected for errors in the
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REFERENCES
1. Strachan MW, Frier BM. Insulin Therapy: A Pocket
2. Banting FG, Best CH, Collip JB, Campbell WR,
Fletcher AA. Pancreatic extracts in the treatment
of diabetes mellitus. Can Med Assoc J. 1922;12(3):141-
145.
3. Forsham PH. Milestones in the 60-year history
of insulin (1922-1982). Diabetes Care. 1982;5(suppl
5. Greene JA, Riggs KR. Why is there no generic
insulin? Historical origins of a modern problem.
6. Pawaskar MD, Camacho FT, Anderson RT,
Cobden D, Joshi AV, Bal Krishnan R. Health care
costs and medication adherence associated with
initiation of insulin pen therapy in Medicaid-enrolled patients with type 2 diabetes:
a retrospective database analysis. Clin Ther. 2007;
29(6), pt 1:1294-1305.
7. Hall JA, Summers KH, Obenchain RL. Cost and
utilization comparisons among propensity
score-matched insulin lispro and regular insulin
8. Hollemen F, Gale EA. Nice insulins, pity about
9. Miller DR, Gardner JA, Hendricks AM, Zhang Q,
Fincke BG. Health care resource utilization and
expenditures associated with the use of insulin
10. Gale EA. Newer insulins in type 2 diabetes. BMJ.
2012;345:e461.
11. Currie CJ, Gale EA, Poole CD. Estimation of
primary care treatment costs and treatment
efficacy for people with type 1 and type 2 diabetes
in the United Kingdom from 1997 to 2007. Diabet
12. Lipska KJ, Ross JS, Van Houten HK, Beran D,
Yudkin JS, Shah ND. Use and out-of-pocket costs of
insulin for type 2 diabetes mellitus from 2000
13. Rosenstock J, Dalley G, Massi-Benedetti M,
Fritsche A, Lin Z, Salzman A. Reduced
hypoglycaemia risk with insulin glargine: a
meta-analysis comparing insulin glargine with
14. Riddle MC, Rosenstock J, Gerich J; Insulin
Glargine 4002 Study Investigators. The
treat-to-target trial: randomized addition of
glarine or human NPH insulin to oral therapy of
type 2 diabetic patients. Diabetes Care. 2003;26
(11):3080-3086.
15. Buysman E, Conner C, Aagren M, Bouchard J,
Liu F. Adherence and persistence to a regimen of
insulin vial/syringe in insulin-naive patients with type 2
16. Kennedy K. States scramble to drive down
http://www.usatoday.com/story/news/politics
17. Sack K, Pear R. States consider Medicaid cuts as
http://www.nytimes.com/2010/02/19/us/politics
18. Cohen D. The prickly problem of access to
insulin. BMJ. 2011;343:d5782.
19. Gill GV, Yudkin JS, Keen H, Beran D. The insulin
dilemma in resource-limited countries: a way
Department of Health and Human Services; 2014.
http://www.cdc.gov/diabetes/pubs/statsreport14
2015
21. Frank RG, Sallee FR. Generic entry and the
22. Fleming T. Drug Topics Red Book: Pharmacy’s
Fundamental Reference. Montvale, NJ: Medical
Economics Co; 2006.
23. Food and Drug Administration. Orange Book:
Approved Drug Products with Therapeutic
24. WHO Collaborating Centre for Drug Statistics.
Guidelines for ATC classification and DDD
25. Brown T. 100 most prescribed, best-selling
June 9, 2015.
26. Cunningham PJ. Medicaid cost containment
and access to prescription drugs. Health Aff
27. Berndt ER, Aitken ML. Brand loyalty, generic
entry and price competition in pharmaceuticals in
the quarter century after the 1984 Waxman-Hatch
dilemma in resource-limited countries: a way
and Customary (U&C) Prices for Commonly Used
29. Kesselheim AS. Rising health care costs and
life-cycle management in the pharmaceutical


