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EDITORIAL

Spending for Diabetes Drugs is Increasing in the United States

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As of 2007, the treatment of diabetes has become the leading source of increased spending on prescription drugs. This was reported by Medco Health Solutions Inc. in its 2008 Drug Trend Report, a comprehensive analysis of prescription drug spending and utilization.[1] In 2007, diabetes drugs accounted for 7% of prescription drug spending in the United States (U.S.). See **Table 1**.

Table 1.
Top Therapeutic Categories Contributing to Drug Spending by Medco in 2007[1]

Disease category	Contribution to overall plan spending (%)
CNS, Neurology, Mental Health, and Pain	22.7
Cardiovascular	22.4
Gastroenterology	9.2
Respiratory and Allergy	9.1
Diabetes	7.0
Anti-infectives	6.7
Musculoskeletal and Rheumatology	5.3
Other	17.6

Diabetes drugs had the distinction of contributing 20.6% to the overall 2.0% rise in prescription medication costs to Medco. Diabetes is now first on the list of the ten greatest contributors to the upward trend in prescription costs. The top 13 diseases in descending order are currently (1) diabetes, (2) respiratory diseases, (3) cancer and transplants, (4) rheumatologic diseases, (5) seizures, (6) viral infections, (7) Alzheimer's and Parkinson's Disease, (8) psychosis, (9) urologic diseases, (10) dermatologic diseases, (11) pain requiring non-narcotic relief, (12) depression, and (13) hyperlipidemia. The basis of this report is benefit data from Medco, the nation's leading pharmacy benefit manager. The data are from Medco's 2007 total net revenues of more than $44 billion, which go toward prescription drug benefit programs for one-in-five Americans.

The overall increase in spending on prescription drugs was low, at 2.0%, during the past year, which the report defined as between 2006–2007. The increase in spending on diabetes drugs increased because of a combination of factors. The number of patients using diabetes drugs increased only slightly, by 2.3%; however, the sharp increase of 9.5% in the unit cost per drug per patient and the large number of patients with coverage for diabetes combined to generate a 12% increase in spending on diabetes drugs. The increased cost per patient can be attributed to a combination of an increased number of patients, a rise in prices of brand-name drugs, and a migration of patients receiving treatment toward newer more expensive drugs.

Increased use of various synthetic insulin products, such as rapid-acting analogs, including Apidra® (sanofi-aventis), Humalog® (Eli Lilly), and NovoLog® (Novo Nordisk), and long-acting analogs, such as Lantus® (sanofi-aventis), and Levemir (Novo Nordisk), contributed to the trend in increased spending. Total sales of Exubera® (Pfizer),

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which was withdrawn from the market in late 2007, contributed very little to overall spending on insulin products. The unit cost of insulin, which also reflects some migration from insulin vials to insulin pens, increased by 14.5% last year. This rise outstripped the increase in the unit costs of oral agents.

Among noninsulin hypoglycemic agents, utilization growth was led by Januvia™ (Merck), which was launched in December 2006. Byetta (Amylin Pharmaceuticals), which was launched in April 2005, also contributed to increased spending in this category. Two recently approved oral combination drugs also added to the growth of this category: ACTOplus met™ (Takeda), launched in August 2005, and Avandaryl® (GlaxoSmithKline), launched in June 2006. Increased spending for all of these drugs offset the decline in sales of Avandia® (GlaxoSmithKline), following release of evidence that use of this drug was linked to cardiovascular disease.[2] Despite a decline in the unit cost for many generic diabetes drugs, overall spending on generic drugs increased by 8.7%.

The Medco report went on to predict that over the next three years, from 2008 to 2010, spending on diabetes drugs would increase by 8%. Such an increase for diabetes would be second only to that for lipid-lowering drugs. New drugs in the pipeline that are likely to be submitted to the Food and Drug Administration for approval include agents from the glucagon-like peptide-1 and dipeptidyl peptidase-4 inhibitor families. Also a combination drug containing nateglinide and valsartan is under development.

Future spending trends for diabetes will likely be affected by multiple factors. Newly approved drugs for diabetes and obesity will probably be expensive. New indications for selected existing diabetes drugs, such as the prevention of diabetes or obesity, will increase use of these products. New dosage forms, such as alternate routes of insulin administration, will offer convenience and possibly better predictability of absorption, but at a cost.[3] New combination products might be released and the costs of these products compared to those of their components might increase or decrease spending for these drugs. Patent expirations and first-time generic introductions will lower overall spending for diabetes drugs. The next diabetes drug whose patent is scheduled to end will be Prandin® (Novo Nordisk) in 2009. Drugs can become approved for over-the-counter use and this tends to lower the necessary spending for the drugs by prescription plans because the expense is generally shifted to the patient. New research and clinical recommendations will affect prescribing patterns and can increase or decrease the costs of prescriptions. Recently reported evidence has demonstrated that colesevelam may improve glycemic control as well as reduce LDL-cholesterol levels in patients with type 2 diabetes receiving sulfonylurea-based therapy.[4] Finally, the increasing prevalence of diabetes that is expected in the next few years will increase utilization of and spending on diabetes drugs.

The use of generic drugs can reduce the cost of medications while continuing to provide effective care. Generics can provide the safety and efficacy of brand-name products at a lower cost.[5] Before a patent on a drug expires and it is produced generically, a pharmaceutical company may launch a newer brand name product containing the same basic ingredient. To extend the patent life of an existing compound, a manufacturer may choose to adopt one or more of the following six approaches:

1. Develop a once-daily, extended-release version of a product. This approach was used for Glucotrol® XL (Pfizer) and Glynase® PresTab® (Pfizer).

2. Introduce a new combination product. This approach was used for Glucovance® (Bristol-Myers Squibb), Avandamet® (GlaxoSmithKline), Metaglip™ (Bristol-Myers Squibb), ACTOplus met (Takeda), Avandaryl (GlaxoSmithKline), Janumet™ (Merck), and Prandimet™ (Novo Nordisk).

3. Obtain a new indication for a product and market it under a different brand name. This approach was used for Revatio® (Pfizer) for pulmonary arterial hypertension, which contains the same active ingredient as Viagra® (Pfizer), but was approved for a different indication at a different dose and strength.

4. Add another molecule to the basic drug to extend its half-life. This approach was being considered by Nektar for developing a long-acting form of Exubera (Pfizer).

5. Develop a single-isomer version of a racemic compound. This approach is being considered for thiazolidinedione products that are currently on the market, such as Actos® (Takeda) and Avandia (GlaxoSmithKline).[6]

6. Introduce an active metabolite of an existing product. This approach is being studied for Combrestatin-A4.[7] This compound is a potential antihyperglycemic agent, and it is the active metabolite of Zybrestat™ (OXiGENE), which is being developed as a chemotherapeutic agent.

At this time, there is plenty of room for improvement in the control of diabetes in the U.S. The latest data from the National Health and Nutrition Examination Survey, reported in April 2008, indicated that between 1999 and 2004, the age-adjusted percentage of people with diagnosed diabetes achieving a hemoglobin A1c target level of <7.0% was 57.1%.[8] In type 1 diabetes, additional drug delivery methods are needed and in type 2 diabetes additional drugs are needed for those patients who cannot achieve adequate results from a healthy diet and regular exercise. Such new drug delivery systems and drugs are in the pipeline. In spite of strong evidence that a healthy diet and exercise program can decrease the incidence of diabetes,[9] diabetes is likely to become more prevalent in the U.S. The number of affected adult patients is likely to climb from the current estimated number, 20.6 million, which is 9.6% of the adults in the U.S.,[10] to as many as 37.7 million by 2031, which would be 14.5% of the projected adult population.[11] It is very likely that spending on drugs for diabetes will continue to increase.

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