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Session 96PD
Prescription Drug Update

Track: Health

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Summary: Pharmaceutical costs typically represent almost 20 percent of the claims cost for group medical insurance. While many stakeholders are reporting recent successes in decelerating the growth of pharmaceutical costs, it is no less important now than it was three years ago to carefully monitor and predict the influence of pharmaceutical costs on future medical premiums. Panelists with close ties to prescription drug benefit programs provide updates on topics, including anticipating the future pace of drug cost and utilization, developments in benefit design, the fastest-growing prescription drug segment—specialty pharmacy, the pharmaceutical manufacturer perspective on drug costs and the evolution of pharmacy benefit managers (PBMs).

MR. KEVIN M. DOLSKY: I'm going to introduce our speakers and go over the format, and then we'll get into our panel. The first panelist will be Christopher Wilson. Chris is going to talk about drug trend. Chris is fresh off the other Disney property in Florida, where he was Monday through Wednesday and where Medco rolled out its 2004 drug trend report. He has current information. For many of you

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Note: The chart(s) referred to in the text can be found at the end of the manuscript.

who have seen this drug trend report in previous years, it's one of a couple of comprehensive studies that have been put out annually on drug trends. It contains some good information and is current. Because it is so current, we were unable to get copies. If you're interested in getting the drug trend report, you can go to www.drugtrend.com.

I'll give you some background on Mr. Wilson. As I mentioned, he's with Medco Health Solutions and is vice president of consultant support. Previously he was with UnitedHealthcare as vice president of sales and account management. Before that he was with Prudential for a number of years.

Our second speaker is Margaret Wear. Margaret is going to talk primarily about benefit design. Margaret is vice president and a pharmacy actuary for PacifiCare Health Systems. She is responsible for all pharmacy actuarial issues for both the health plan and prescription solutions, PacifiCare's PBM. Before joining PacifiCare, Margaret was chief actuary at the country's largest PBM, where she was responsible for assisting clients with prescription drug, Medicare reform and risk issues, including plan design and drug trends. Margaret is one of a small number of actuaries in the United States who have been concentrating on pharmacy issues for the past several years.

Our third speaker is Terri Bernacchi. Terri is a pharmacist and also has an M.B.A. Terri's angle is a bit different from what we sometimes hear. Her business is working primarily with manufacturers. Terri is president of Innovative Health Strategies (IHS), a business solutions provider that affords pharmaceutical manufacturers assistance with their rebate agreements. The company has been in business since 1995. Before founding IHS, Terri served for four years with Blue Cross of Wisconsin, where she oversaw pharmacy services, worked with employer groups, managed rebate contracting and chaired the pharmacy and therapeutics (P&T) committee. She additionally has been in physician practice management and hospital and specialty sales for a pharmaceutical company and was the hospital pharmacist in an acute-care hospital.

I have a couple of comments with regard to the format of this session this morning. This is a panel discussion, so the panelists will speak first. After that we'll have time for question and answers.

MR. CHRISTOPHER P. WILSON: The year '03 was extremely interesting for us. In '03, from a pharmacy standpoint, there were a number of initiatives that we found to be impacting on what happened with trend. For example, there was the women's health initiative that came out last year regarding hormone replacement and what that did was specific utilization in a specific therapeutic class. You'll see what happened in that therapeutic class after those findings came out. There were a couple of important over-the-counter (OTC) transitions. I'm thinking specifically of Claritin and of a specific strength of Prilosec. You'll see what happens when something like that occurs. I have an example of what happened to Claritin in the

middle of last year because of the OTC. Finally, there were a number of significant generic conversions, and we can show you what happens in a managed environment when a drug goes from brand to generic, and the impact it has on cost and utilization.

I'm going to mostly show you Medco data, but I'm going to start with some Centers for Medicare & Medicaid Services (CMS) data. The good news is that drug trend is slowing down, but unfortunately it remains the highest in terms of general health care. I'll talk about where we see trend going from the Medco perspective. It's not all that different from CMS. CMS data projected drug trend to be at 13.4 percent last year.

We had a little different experience. I want to share with you what we're seeing and let you know that there are ways to mitigate trend. There are techniques our payers have adopted and that we've done with them, as other PBMs do as well. Our joint trend in '04 is 10.2 percent. It's the third year in a row we've seen a drop. More than 50 percent of our clients are on an integrated basis, and when we say integrated, it means mail and retail. At that point, more than 50 percent of our clients had trend in single digits, and our meeting trend was 9.6 percent. We're happy with that, and, more importantly, so are our clients.

Where's trend coming from? Trend drivers have changed over the past three years. In '01, utilization was the most significant driver. In '03, that changed. The significant driver was inflation. Here's some background. The brand-name drugs' average wholesale prices were up 6.5 percent in '03, while generics were up 2.3 percent. That's offset by what's happening in mixed. Mixed is shrinking, showing 2.9 percent in '01, 2.8 percent in '02 and 1.9 percent in '03. What's happening is more drugs are going to generic. As you'll see later, the pipeline for new drugs is shrinking. The number of new users is also dropping to a degree. Current users are getting more therapy, but there are not many new users coming on.

What drives our spend? I want to clarify spend and trend. This is our spend (see Chart 1). For the first time CNS (neurology, mental health and pain) is bigger than cardiovascular. This is our data. For background these data are approximately 94 percent based on $32 billion of spend. They're on integrated accounts. What we experienced for the first time with CNS drugs were bigger percentages of spend than cardiovascular. Why was that? We think there are more generics being used on cardiovascular. We also saw a lot more utilization by kids in CNS. In CNS more behavioral medications are being given to kids, which is not necessarily good news.

In terms of trend drivers, this is different. The good news with rheumatological is that while it's a big driver, it's not a big piece of the spend. Nevertheless it's having significant unit cost increase. These unit cost increases are coming basically from Enbrel, which is an injectable and is expensive. Regarding the anticoagulants, there's something called Plavix. It's used to clear up bloodstreams.

Let's discuss some of the negative trend drivers. In the anti-anxiety area we saw a major increase in the number of generics. Estrogen and progesterone saw a drop-off when the women's health initiative came in, and we saw that the utilization of those specific drugs in the therapeutic category dropped significantly. Last and certainly not least is the allergies category (see Chart 2). When Claritin went from a prescription to OTC, look what happened to Claritin prescriptions from the first quarter of '02 to the first quarter of '03. They went from 1.85 million down to approximately 250,000. When things like that happen (it happened with Prilosec and I think now there's talk about Statin going OTC), it has a significant impact on trend and for that matter on spend. We work closely with clients on that. When something comes up, how do you move to identify those users and to get them OTC? Do you have a specific strategy to make that happen as quickly as possible?

Drivers of trend obviously vary by age group (see Chart 3). An interesting thing from our perspective is that in the 0-to-19 age bracket, utilization is on a per month per member (PMPM) basis. It's much higher than it is in the over-65 age bracket. I talked before about behavior and kids. We found that 5 percent of the kids aged 0 to 19 take at least one drug for a behavioral issue, be it attention deficit or depression. The spend is up significantly in the 0-to-19 age bracket. The good news in the 0-to-19 bracket is we've seen a big falloff in antibiotic usage. I have four kids. I remember you went every other day to get an Amoxicillin or Augmentin for your kids' earaches. That's not being done as much anymore. What we find is kids are on acute drugs, so they are taking a lot more brands. Regarding the older people over age 65, while their utilization is high, they are also taking a lot more generic drugs for maintenance.

When you look at the spend breakdown by age group (see Chart 4), the 0-to-19 bracket has the highest spending on respiratory and allergy. We're seeing a lot more biotech for asthma. That's obviously going to boost cost as well. At the other end, cardiovascular is a bigger piece for the older population.

I want to move to an area that has emerged in the PBM world, and that's the use of specialty drugs. These are expensive drugs. They're used for a smaller population, although cancer is certainly a focused area. This area is seeing a tremendous increase in spend and trend. It's increasing every year in the overall spend. It's an area in need of management because when you're the payer, an employer sometimes is dealing with biotech and specialty drugs under the medical piece. It's trying to move it into a more managed piece, perhaps under pharmacy. Often there are a lot of moving parts, and you'll see in a second that the biotech pipeline is robust. More of these drugs are coming into the marketplace from an unmanaged perspective. They are going to drive cost and increase trend. Every PBM is focused on this, and everyone is creating specialty divisions by purchasing or acquiring companies to focus on it.

From a spend standpoint, the highest spending is predominately in multiple sclerosis (MS) and rheumatoid arthritis (see Chart 5). Arthritis is a big trend area.

Enbrel, which is an expensive injectable, is about 50 percent of the trend. You'll see going forward that a lot of drugs for cancer, MS and growth hormones are in the pipeline, with more to emerge.

There is some good news, though, and that is generics. This is our book of business. I've seen that you want to get to a 40 percent threshold of generic dispensing. In '03, we experienced almost 44 percent. The way we look at generic dispensing is that every 1.5 percent increase in generic dispensing saves about 3.5 percent in spend. We are focused, and I know every PBM is focused, in making sure that generic education is available to the payers, the members and the physicians.

Some of the key generics that came out in '03 were Wellbutrin and Paxil. Paxil was almost $2.2 billion in terms of sales in '02, and Wellbutrin was almost $1.5 billion. When they go generic, they have a significant impact on the bottom line. Keep in mind that no one is caught by surprise anymore when new drugs enter the marketplace or when drugs go off patent. Every PBM and every health plan is out there managing the pipeline. We know when something goes in for the first time. We know when something is in the first phase of clinical trials. We're following it all the way, because it's not only a cost implication; it's also a coverage implication. We're tracking it.

We have a specific division, as do my competitors, and that's what it does. It tracks the drug from beginning to end. When a drug goes generic like Paxil did in September '03, we went in literally four months and started doing the generic dispensing. We're at more than 80 percent for mail and close to 80 percent for retail. This happened with Prozac. It's something that everyone does because it is so important for the payer to enjoy the generic savings.

I'll talk about where we see trend going forward. CMS' projection is different from ours. CMS is projecting trend in '04 at 12.9 percent and sees it dropping to 12.1 percent in '06. Over the next 10 years, it's projecting drug trend to be approximately 11 percent and sees it dropping to 9.2 percent in '13.

As you do these projections, you have to weigh a couple of things. That's why it's so important to have your pipeline management and to understand who in your membership is utilizing drugs such as Zocor and Zoloft, which are coming off patent soon. You need to understand who's in your pipeline in terms of the specialty. This is the way we see it.

Year	2004	2005	2006
Utilization increase	4% to 6%	4% to 6%	3% to 5%
Price and mix increase	5% to 7%	5% to 7%	6% to 8%
Annual total drug trend increase	9% to 13%	9% to 13%	9% to 13%

These are ranges over the next three years. They're probably conservative, but those are the ranges that we see. They're consistent with what we've seen over the past two years. We see it leveling off. Sometimes you're going to see a spike, because some of those drugs that you thought were coming off patent and were going to generic don't. Perhaps those organizations have good lawyers, and they may be able to extend the patents. They may find new indications.

What's going on with the FDA approvals is interesting. There are fewer new drugs coming to the market. When the new molecular entities (NMEs) start slowing down and coming out, the mix decreases as a component of trend. The number of applications is dropping to a degree. This is somewhat good news, but what we're concerned about is that the specialty and the biotech are more robust in terms of drugs that are in the late stages. They are going to have a significant impact. They are expensive and draw on a smaller population, but it's something to be aware of.

There are a couple of blockbusters that are sitting out there, such as Arcoxia. There are approximately 300 drugs in phase three of clinical trials. We're seeing a big focus on cancer drugs, specifically as they relate to specialty as you can see in Chart 6. At the bottom are small populations. I'm not talking about orphan drugs, but the smaller populations. There is a huge unit cost. That's why we're concerned about specialty as is the entire industry. Healthcare companies will be coming to us. This is an area that needs a tremendous amount of focus. It has been a focus for the past two or three years.

The good news is there's about $25 billion that could expire by '06. We say "could" because there are always the legal ramifications that someone may get into and prolong things for at least a year or two. I looked specifically at Zoloft, which is a $2.5 billion drug, and Zocor, which is $3.3 billion. Those are two significant drugs that we anticipate coming off patent. Again, we're not sure about the pipeline on the other side. We think this is impacting on the '09 to '13 projection.

As a payer, your hands are not tied in what you can do to offset trend and offset spend. As a payer, you should never sit on your hands when it comes to any benefit, especially pharmacy. There are so many moving parts. My background is health care, and while that is a complex area, pharmacy is three times more complicated. The CMS trend in '03 is projected to be 13.4 percent, and our book of

business was integrated at 10.2 percent. We had 50 clients that changed last year. They limited the number of refills allowable at the retail pharmacy to two, three or maybe four. After that the prescription immediately goes to mail. At mail the economies are stronger. We're acquiring drugs as does every PBM that has mail at a much lower rate. The acquisition cost is much lower, and it's tremendous in terms of what it does to trend.

Limiting refills at retail is just one of the things people can do. There are a number of other tactics I'll talk about in a second. While trend is double-digit in general, there are ways to reduce it significantly. It's something to be aware of. I know a number of you are with carriers and in the consulting world.

This is the way we're looking at things going forward. It is a new healthcare economy. A number of things are happening, which we'll be talking about in some of the panel discussions. Part of it has to do with the way we look at things. We like to think that we're realists and that our clients are realists, and we want to adjust the sales going forward every year because here's what is coming down the pike. We can have more than a 90-minute discussion on what the Medicare Part D means to payers. What does it mean to PBMs? What does it mean to other organizations? Is it Medicare, medication reimbursement on Medicare Part D or new benefit options?

What is health savings account going to mean? What about the tax breaks on OTC purchases and the fact that you can put them through your flex?

Obviously the advances in technology will be important. Specialty pharmacy has emerged and is growing. You have pharmacogenomics, and the ability to figure out which drug you should take and which one is going to have the most effect on you, which is fascinating to me. Something as simple as electronic prescribing will be important. That's the way we look at trend. That's the way we're projecting what we see in the future. That's the Medco perspective.

MS. MARGARET WOOD WEAR: I'm going to talk briefly about developments and benefit design. In pharmacy benefit design, we're seeing three-tier co-pay plan designs, which seem to have become the most common plan design; drug management tools, which are more widely accepted; four-tier plan designs; consumer-driven plan designs; and plan designs using reference pricing. Most people probably understand what a three-tier plan design is because it's been around now for quite a few years.

The drugs are usually divided into three buckets: generics, preferred brands or formulary brands (sometimes different plans use different terminology) and nonpreferred brands or nonformulary brands. The co-pays are set for each of those tiers to incentivize the member to choose generics or preferred brands. The preferred brands are selected based on cost-effectiveness, so that if a member utilizes the preferred brand, that's a better cost outcome for the member and for

the plan.

Some alternative plan designs in looking at three-tier set their buckets a little bit differently, where they might put lower-cost generics in the first tier, and if there are some truly low-cost brands, they also might be in the first tier. Higher-cost generics and the rest of the preferred brands might be in the second tier, so you would end up paying slightly higher co-pays for some generics that are higher-cost brands.

When we look at drug management tools, and a lot of plans are using these much more aggressively now, we generally look at five categories: higher authorization, step therapy, managed drug limitations, generic incentive programs and mail order. One more these days is probably your use of OTC and incentivizing that.

Prior authorization is a program where a member has to have a physician call in to get authorization for this prescription to be filled. Specific medical criteria might be required before the use of a specific drug is approved.

Step therapy generally looks at and perhaps requires the use of a lower-cost therapy before moving on to a higher-cost therapy. You see this a lot in categories like pain, where there are less expensive pain medications such as nonsteroidal anti-inflammatory drugs (NSAIDs), which include drugs such as ibuprofen, instead of moving up to a higher-cost pain medication like a Cox-2, which might be a Vioxx type of a medication. Even now, as Chris was talking about the rheumatoid arthritis category, sometimes you see cases where the pain categories often are used first on rheumatoid arthritis and then you move to the higher-cost products like Enbrel or Humera.

Managed drug limitations are the limitations of what can be filled. Sometimes a length of therapy is limited or the number of pills is limited. If you look a drug such as Imitrex, you might be limited on the number of what you can fill in a month.

Generic incentive programs include things like mandatory generic or programs where the member is required to pay the difference between the cost of a brand and the cost of the generic if he selects to have the brand filled. It may be as simple as setting your co-pays appropriately to incentivize generics.

Mail order, as Chris said, is a significant savings in certain plans. There are a number of ways to incentivize mail order. Co-pay plan design is one way, where you don't require a full three-month co-pay even though you're filling a three-month prescription. That frequently incentivizes the member to use mail order. You can also require members to use mail order after a certain number of fills. Perhaps a first and second fill are allowed at retail and then there's a requirement that the fill go to mail order when it's a long-term maintenance drug.

Four-tier plan design is usually set up like three-tier plan designs where the first

three tiers are generics, preferred brands and nonpreferred brands. The fourth tier can be drugs that might otherwise be excluded. Sometimes the member even is required to pay a 100 percent co-pay, but he still gets to enjoy the discount that the plan has set up in his network. Other four-tier plans look at putting high-cost drugs in that fourth tier, and then they would charge a high member cost share such as a 50 percent coinsurance. Biotech drugs and those types of medications would fall into this tier.

There's also a four-tier plan design that's similar to a defined-contribution plan design. Rather than requiring the member to pay a co-pay, the plan will cover up to a certain dollar amount on the fill, and the member has to pay the difference. The plan might cover as much as $40 on a preferred brand, but if the brand costs more than that, the member pays the difference between the $40 and the actual cost of the drug. It's generally tiered so that the plan pays less at the higher tiers, which encourages members to use the generic or the preferred brand.

In looking at consumer-driven plan design for pharmacy alone, it's usually set up in different stages. I'm not sure how many of you are familiar with the way regular consumer-driven health plans work on the medical side. It's similar to that. At the first stage the employer funds a pharmacy savings account on an annual basis, and the employer gets a say on what this plan design should look like. When the member uses the full amount of his pharmacy savings account, it bumps up into a second stage. In that stage it's like a deductible. The members uses his pharmacy savings account, and then there's set amount that he has to pay such as a deductible. He pays all of this amount in this bucket.

If he gets beyond that into the third stage (he's had to use his full pharmacy savings account and pay his deductible), additional prescription coverage after that is provided under some standard benefit design. The plan design is then determined by the employer. The thought process behind this type of plan design is that because the member has control over what he spends his pharmacy savings account on and what he's spending the deductible on, he'll make better, more cost-effective choices when choosing his drugs.

When you look at reference pricing plan design, you see two basic designs. Plans will establish a reference price in each class of drugs. In one type of plan design the plan will cover up to the amount a drug costs at that reference price. If the member selects a drug that's beyond the reference price, he has to pay the difference between the reference price and the cost of the drug that he selected.

Another plan design is also based on a reference price, and the reference price is determined in each therapeutic class. Rather than requiring the member to pay the difference, the plan sets co-pays based on that reference price. If it's a generic and below the reference price, it's going to have a co-pay. If it's a generic and above the reference price, it's going to have a higher co-pay. The same is true with brands. There will be two co-pays for brands based on whether the drug is above or

below the reference price. I think it's a little confusing, and I think it's a new plan, so I'm not sure what the results have been. If the results are good on this plan, we may be seeing more of it. I don't know right now.

Let's talk about specialty pharmacy, which Chris brought up. We usually see this as high-cost, low-utilization drugs. They do require special handling. When you look at specialty drug pharmacies—a lot of the PBMs now have specialty pharmacies, and I think some still are not affiliated with PBMs but probably have contracts with different PBMs and others that are filling these types of prescriptions—it's not just mail order. It's not a matter of submitting a script and they send it to you. There are a lot of other services included with a specialty pharmacy because of the nature of what these drugs are.

They include care management services, which incorporate case review based on medical guidelines; outbound calls to clients, in which someone calls the individuals who are receiving these medications and talks to them before sending the medication out to be sure that the member is home to receive it (these drugs require special handling); scheduling delivery of medication so that they are certain that the member is where the medication can be received; pharmacist counseling to members who have questions about their medications and how to use them or questions about side effects; and compliance monitoring because they want members to stay compliant with them.

Specialty pharmacies also usually include disease therapy management programs to work with members so that the members receive information about their diseases and how to best control them. Because they are going through a PBM specialty pharmacy, as Chris referred to, there are generally savings from these pharmacies, as well as better outcomes based on the case management that's provided.

MS. TERRI BERNACCHI: How many people here own shares or stock in pharmaceutical manufacturers? How many of you have 401(k) programs that are invested in money markets? How many have retirement savings accounts? The reason for my asking that question is that I work for the pharmaceutical manufacturers. I started my company in '95. I've worked for a number of different places that don't all connect unless you know my background.

I'm a pharmacist. I worked for nine years in a hospital. I then worked for a pharmaceutical manufacturer as a sales representative in Madison, Wis., which is tightly managed care. I worked for Bayer when Cipro came out. I worked for Aurora Health Care, which is an integrated delivery system. My job there was to call on physicians because I had learned how to do that as a sales representative. I became involved in understanding how medicine works.

From there I wanted to get back into pharmacy, and so I worked for Blue Cross/Blue Shield of Wisconsin, and I thought my job there was going to be

utilization review and working with employers. What it ended up being was negotiating rebate agreements with pharmaceutical manufacturers, which I had an empathy for having worked for one in the past. The reason that I'm here today is to talk to you about why what's good for pharmaceutical manufacturers is good for all of us.

Because you are all shareholders ultimately in the U.S. pharmaceutical industry, I think I can take that mantle and talk to you as shareholders in this industry about why what's good for pharma is good for all of you individually.

What I wanted to do was give you as shareholders of the pharmaceutical industry talking points to others so that you can see some of the things that are going on in this industry and you can maybe relate to them a little bit differently than as a consumer. I'm going to briefly go through how big the industry is and show you some statistics, some of which might be familiar and some of which may be new. I'm going to talk about three particular pressures on this industry of ours.

It has the pressure to innovate, which is to continuously invent new things. We heard in the presentations about some of the innovations in this industry. We need to know what drives that innovation and what stifles it. The second pressure is profitability. Pharmaceutical manufacturers like any other company are in business to make profit and build value for the shareholders. The shareholders are the people like us. There are also stakeholders, who are the consumers of the goods that the manufacturers produce, invent and develop. At the same time, we need to make sure that the innovations that they develop are affordable.

There are compliance issues for this industry that are different from other industries. We'll go through that later. Do most of you know about Sarbanes-Oxley? It's the Enron legislation, which basically means the CEO or the CFO has to sign off every quarter that everything is working fine. Pharma has some issues that pertain particularly to Sarbanes-Oxley. There are also some marketing and sales guidelines that the Office of Inspector General has put out that create some interesting challenges for the pharmaceutical business. Drug manufacturers can't do business as they have done it in the past. Obviously there are FDA rules and regulations.

How does what happens to pharma affect all of us as shareholders and as people? We know that this industry has innovated a lot in terms of prescription drug products that have cured disease. About 10 years ago, AIDS was a death sentence. Now it's a chronic disease. People will be on these medications for life, and their life could be decades as opposed to a few years. We educate as an industry the physicians, the pharmacists and the nurses. We support medical education strongly as a pharmaceutical industry. We've historically had a positive effect on the balance of trade.

I think most people would agree if they know the pharmaceutical industry that there's a philanthropic aspect to what it does.

There is an incredible amount of pressure on this industry. It's everyone's favorite target if you listen to the media discuss the pharmaceutical empire. I'm not going to make any apologies because I do know that there has been some misbehavior in this industry as in any other, but there's a lot of pressure that's affecting the viability of some of these pharmaceutical manufacturers.

One statistic that people frequently cite or believe is that U.S. citizens use more and spend more per use than the rest of the world. That's not necessarily true. I tried to disprove it. One of the problems is that the same products that require a prescription in this country may well be OTC in Mexico, Canada or other countries. You don't do a comparison that's direct on a product basis. The Kaiser Family Foundation noted in '00 that there were an average of 10.8 prescriptions per person in the United States. I can't tell you how that compares with other countries, again because some medications are OTC in other countries.

One of the comments about this industry is that we have more flexibility in the United States with regard to our choice in health care and our prescription drug choice. It's greater than in any other country, but there's a cost that goes with that. It is one that we're bearing for the rest of the world.

IMS collects international and national data on the market. The pharmaceutical industry is a true international industry. Global sales through pharmacies in 13 markets through August of last year were growing at 7 percent to about $300 billion, which was a projected $450 billion for '03 altogether. The United States pays the lion's share of that. As of '02 it was 51 percent, and in '05 it's going to be 60.5 percent of the sales for the entire world.

One of the other comments that I want to make is in terms of how big this industry is. Pharmaceutical manufacturers have hired some of the best and brightest. More than six out of 10 pharmaceutical workers have professional degrees or PhDs, which is twice the number for all other industries combined. Pharmaceutical medicine manufacturers provided about 300,000 wage and salaried jobs in '02. That's an understatement because that's just the direct employment. There are lots of little companies like mine and other industries and entities that live off of what the pharmaceutical manufacturers are doing by providing services and support to this industry.

The hourly earnings of people who work in the pharmaceutical and medicine manufacturing industry exceed that of other industries. Some of the top-paid jobs in this industry are projected to grow in the 20 percent and 30 percent range in the future up to '12.

I'm going to go through the challenges now. The key challenge is research and development (R&D). As you probably are aware, pharmaceutical manufacturers must be able to justify the cost of developing the product. After you start the R&D, only one out of 10 products—or if you read some places, one out of 100 products—

will ever get to market. All of the pharmaceutical manufacturers are looking for that billion-dollar blockbuster. They tend to not put time and money into developing some of these smaller products that won't yield the payback because the patents expire. I didn't include it in this presentation, but there's a fairly compelling diagram that shows it's between 12 and 16 years to bring a product to market, and then you have only a few years left of patent life. As Chris said, when the product hits the end of its patent life because of managed care, basically it goes away.

Pharmaceutical manufacturers are always looking for ways to develop that intellectual property, protect it and reduce the copycat branded products. The global industry is a problem in that in the United States, you can't infringe on patents of a branded pharmaceutical product and get away with it. Globally there are some countries, notably India, Brazil and China, that are taking our patented products and creating copycat products. They sell those products either as true counterfeits or as drugs that are close to the same thing and these sales do not benefit the pharmaceutical manufacturer. There are some trade problems associated with this. Obviously the generic manufacturers reap the benefit of all the R&D fairly quickly.

The bottom line is that the other countries have more highly regulated and fragmented healthcare systems. They tend to have cost controls or price controls, so they have failed to stimulate the growth to the same extent as the deregulated U.S. environment. This is the only free market for pharmaceutical products in the world. Everyone else has some type of price control and governmental decision-making body that determines whether or not your product will be on the list of approved medications and at what price you'll be able to participate. Different countries do this in different ways. It's one of the reasons why it's hard to drive a true comparison between us and specific other countries.

We're no longer in a positive trade balance on prescription drugs. You should think about that with regard to the pressures when pharmaceutical manufacturers are forced to sell products at lower than U.S. prices.

Yesterday there were hearings in the Capitol about whether or not to allow Canadian imports. I don't need to emphasize the detrimental effect of allowing that type of thing on this industry. One of the reasons for the trade deficit, in addition to the inflated value of the dollar, is that technology in particular and a sharp increase in pharmaceutical imports are driving some of this trade deficit. From January to February of '04, the imports far exceeded our exports. That's a trade deficit of about $2.5 billion per month.

The second challenge that I'd like you as shareholders to be aware of is profitability. Pharmaceutical companies are like any other company. They need to be able to drive demand and sales volume. They have to be able to address competition. Sometimes the competition has a product that is significantly better, and sometimes it's clinical hair-splitting. I think that one of the things that the

pharmaceutical industry would complain about is some of that hair-splitting results in less access to managed-care entities like PBMs.

They have to worry about the cost of goods sold and the type of manufacturing facilities that you need to be able to create a biotech product that has to be FDA-approved. Implementing good manufacturing practices is an expensive proposition. It's not the same as a facility that's relatively low-tech, such as a business.

They have the cost of sales, which includes marketing and administration. It's a complex sales and marketing channel. You can't just advertise, although they do advertise to the consumer. You have to get to the physicians and some of the other entities.

They need to be able to have a realistic price per unit, but in the face of pressure from constituents, it's hard to make a profit when people are sick, and they want the product at the lowest possible price. There are also relatively few opportunities for big blocks of products.

I want to make sure that you as shareholders understand that this distribution model is not the same as other products. I'll use the doughnut shop as an example. If you are making doughnuts and want to sell to the consumer, the consumer just needs to know where to buy your doughnuts. It's a little bit more complicated as you grow as a company, so maybe you want to go through a wholesaler or distribution channel. The wholesaler or distributor will assist you in getting to the consumer. But it's more effective if you can manufacture your product, get it to a wholesaler or distributor, and the wholesaler or distributor gets it to your retailer.

The pharmaceutical industry is no different from other manufactured goods industries in this regard. Where it differs is the pharmaceutical manufacturer can't go to the consumers for them to make the decision that they are going to take Zocor. The patients, or the consumers, have to first go through the physician, and then if they have a third-party benefit plan, they have to make sure that the benefit program or the payer, whether it's the government, the private sector or the PBM, is going to allow them to have that Zocor and at what price.

PBMs provide a tremendous value in that they can aggregate those payers and those buyers together and negotiate directly with the pharmaceutical manufacturer to get a price that has a benefit to the payer and ultimately to the consumer. Regulators also are involved in approving how some of these relationships work, so you have that level of complication, as well. We heard a few minutes ago about some of the specialty pharmacies, so you need to work with specialized possession takers.

This is the most simplified I can make this. If you look at the contractual relationship based on price and at distribution in this industry, where people take ahold of the goods, one of the reasons that prices in the United States are higher

than they are in the rest of the world is that there are a lot of people in the middle who make a margin, and their business viability and profitability are based upon the price of the drug that they are either dispensing or promoting and paying through a managed-care channel. A large percentage of the average wholesale price or the list price of the drug is not going to the manufacturer at all. It's paying the distribution channel and the payer channel.

In terms of profitability again, pharmaceutical manufacturers have tremendous pressure from Wall Street. Wall Street is either overly exuberant in terms of their news about a new product or is pessimistic. The stock prices can drop tremendously based on news that may or may not be actual (ImClone is an example of this). Again the industry itself is unfortunately focusing on big disease, not necessarily on disease that has no cure already out there because they are looking to make the money back. It's the pharmacoeconomics of the disease. Increasing globalism is having an effect on whether or not pharma will be able to do this.

On top of that in terms of profitability challenges, you as a pharmaceutical shareholder need to remember that the payer is out there with cost-containment tactics. Part of this, which you saw in Chris' slide, is built on use and part is on price. People are using more drugs. People are using more expensive drugs, and the pharmaceutical manufacturers obviously have to set the price. However they are also facing pressure from the payer in terms of whether or not the product would be covered in their benefit. There also are mandated price controls, and we have numerous examples of that.

These price controls have a negative effect on R&D, and that's where our U.S. pharmaceutical industry historically has excelled above the rest of the world. There also are restrictions on reimbursements, which affect your ability as a pharmaceutical manufacturer to garner sales in the marketplace (for example, higher co-pays and generic mandates).

In Madison, Wis., when I was a drug representative, I learned about some of these things. For example, some of the managed-care plans had limited the ability for your representatives to get to the physician. There may be a lack of access. They may have control over the message that the representative takes to the physician.

The Claritin example was an example of a product that a manufacturer was forced by public pressure to take OTC as opposed to having it in a benefit program. There's a different set of requirements for marketing a product OTC than for marketing it as a prescription drug, and that's an unprecedented issue for pharmaceutical manufacturers. There are import regulations. Some of the states are pushing the importation of drugs from Canada. That's unheard of, as well. I can't think of another example where our legislators have promoted the use of a price-controlled product coming into this country over the industry that is resident in our country. You also have new purchasing groups, Medicare drug cards and state coalitions.

I'm going to go through the third challenge relatively quickly because I think you all understand it. This is compliance. We talked about Sarbanes-Oxley before. The purpose of Sarbanes-Oxley is transparency for shareholders. Pharmaceutical manufacturers are accountable to you as shareholders in terms of whether or not they are accurately allocating many of the discounts that I was explaining before that go through all of these payer channels.

These rebates are difficult for the pharmaceutical manufacturer to be able to project. How do you know what the actual rebate is going to be if you haven't gotten the rebate invoice from the PBM for six to nine months? You have to put some accruals aside, and those accruals are large. They may be as much as 20 percent of your gross sales. You need to know and be able to estimate how big those rebates are going to be so that you can have accurate financial statements for your shareholders.

This is a huge issue for the pharmaceutical industry particularly now because you have the Medicare discount program, coming up next month. How big is that discount going to be that they need to be able to book? There are legal threats. If you read the *Wall Street Journal,* you see whatever latest legal threat there has been either against the pharmaceutical manufacturer or against the PBM, which by inference includes the pharmaceutical company. Whether or not their prices are fair, there are a number of federal laws regarding how you have to offer a price to the same class of trade. I think that probably there are more lawyers who work for pharmaceutical companies than PhDs, biochemists or pharmacists.

I think you probably have seen the Pfizer/Parke-Davis Neurontin settlement or TAP Pharmaceuticals with Lupron. There are a number of these multi-million dollar penalties. When the pharmaceutical manufacturer has to pay that penalty, it's going to end up embedded in the price of its next product or for U.S. shareholders in the profitability of the company.

Tom Scully, at an NDC forum, was quoted as saying, "In the next two to three years, health care will change in ways the pharmaceutical industry cannot yet understand. Medicare Part D is one of them." He states that it will be the driving force for the pharmaceutical industry. I basically agree with what he says in that regard. I think that one of the things that's going to happen is that we're heading more toward consumer-driven health care. Pharmaceutical manufacturers and PBMs have an opportunity whereby if they can work together, they can maintain product access to patients so that it's beneficial for both sides. The government is getting more involved.

Where is this all going? I think that cost-shifting is something that's happened in the past. I don't know how many of you remember what happened with prices when they mandated best-price rebates and discounts to the federal government Medicaid programs. Does anyone remember that? Prices were going up in '92 and

'93 12 percent to 15 percent. Cost-shifting happened basically because the states were getting the best price, and to make up the difference the pharmaceutical manufacturers raised their prices to the private sector. That will happen again.

Whether there will be fewer or more rebates is an interesting question. Because as the co-pays under your benefit program are raised, if the co-pay level is $50 for a product, and the cash price the pharmaceutical manufacturer is marketing it for is $48, why would the pharmaceutical manufacturer pay a rebate to a PBM or a health plan? It doesn't make any sense.

One of the problems that the PBM industry has now is that a large part of its revenue stream is associated with these rebates. It could be interesting to see how this shakes out. If you look at what's going on with employers and how the benefits are being challenged, as a small employer myself, I had a 30 percent rate hike a couple of years ago. This past year it wasn't as bad, but there comes a point in time when you can no longer afford to underwrite insurance programs. I can't predict how the prescription drug benefit fits in with that if the pharmaceutical manufacturers continue to have these challenges will they raise prices or have fewer rebates.

The patient will get into more consumer-directed options, and pharma will try to take this opportunity working with cutting-edge PBMs to try to go directly to the consumer and allow those benefits and those rebates to go to the consumer as opposed to the health plan. The biggest effect that I think there will be on the industry if the industry has to tighten its belt goes to academic institutions and the research dollar. Research dollars will be more pinched than ever before, and the support for education will be squeezed. Many medical conferences, pharmacy conferences and nursing conferences are underwritten by grants and donations that are received by the pharmaceutical industry. As they tighten their belts and because of restrictions that the government has in how they market their products, they may do less of that.

MR. CHUCK MILLER: Terri touched briefly on rebates, and I'd be interested in Chris' and Margaret's view of what you anticipate happening with rebates under the Medicare Part D program. Currently rebates are essentially calculated on a retrospective basis, which seems to work fine with fixed-dollar co-pays, but under co-insurance design, you're unable to pass the value of that rebate back to the consumer. Do you see rebates essentially going away or being rolled into the discount?

MS. WEAR: Currently my understanding is that it's still up in the air. I think that at some level we're going to have to pass those rebates along to the member at the point of sale either through the discount that we're going to offer, or through some estimated way.

MR. WILSON: Yes, I'd agree with that. The technology is there if you want to do

that today, and it's probably the fair way to do it if you have to have a coinsurance arrangement. There's so much up in the air about Medicare that it's difficult to say it's going to be this or be that. There's a lot more to come on that.

MR. JOHN R. GOVERNALE: The question I have is as we move into the next phase of the tiering of drugs, that fourth tier from what I understand is going to be a class of drugs that is not predicated on the price of the drug, but the type of drug—for example whether it's an injectable or another type of drug. Is there going to be any issue with discrimination if that's the type of drug that's in that fourth tier and it's a medical necessity that will help the patient? In the first three tiers it's predicated on price. There might be a generic available. There might be a number of brands. Now we get to the fourth tier, and there's nothing else. There's a large co-pay put on that. How is that going to affect the patient and that outcome?

MR. WILSON: I would say when you've seen one four-tier plan, you've seen one four-tier plan. I say that because I've seen a couple of approaches on four tiers. One is lifestyle. They create a fourth-tier for lifestyle drugs that aren't usually covered. I'm thinking of Viagra. What I've also seen on four tiers is where they take brand and make a decision that higher-cost brands are going to go into tier one, and then lower-cost brands are going to go into tier two.

There are a couple of questions that raise a lot of issues. There are always the one-offs that have an appeal process, whereby a member can't tolerate drug A and has to take drug B, but drug B costs $30 more. Those issues get appealed through the payer to the PBM. People always balance in the P&T committees as to efficacy, outcomes and cost. I think it's difficult to say there's a blanket answer to your question because so many different scenarios could occur.

MR. STEPHEN P. MELEK: I have a couple of questions. Chris, you referred to the growth in central nervous system drugs for kids. I've certainly seen that in teachers suggesting to parents that their kid should take ADHD drugs. I think one of the highest-growing utilization classes is kids under five. I am not a shareholder in the pharma industry. I'm more concerned about the misuse of some of the drugs in our population at solving some of those problems.

Related problems are primary-care physicians prescribing antidepressants without proper education and the poor patient adherence rates we're seeing with antidepressants. This could represent a lot of wasted money in the healthcare system. I'm interested in what any of you are doing regarding the antidepressant education of primary-care physicians, of the families that are taking them and the kids who are on them. If we're getting our kids on these central nervous system drugs at such a young age, I heard a psychiatrist say yesterday that there is no long-term study on what these drugs are doing to kids and on what's likely to happen to them down the road. I'm interested in your comments on that.

MR. WILSON: I have four kids, and I'll say first and foremost I share your

concerns. In terms of working with the primary-care physicians, as a PBM we have limited connections with them. We can work with payers to do something along the lines of step therapy or prior authorization—requiring that they go one route before they can go on to the next route. We're in the same boat. There are limited studies of long-term utilization of these types of drugs. Right now, as long as they're prescribed, we have to adhere to them unless there's a protocol in place to stop that utilization. It's a valid concern, and it's something that jumped out at us when we saw that 5 percent of children are on at least one behavioral drug. I hate to say it, but I think it's a reflection on society.

MS. SUSAN MATEJA: Have you seen many dollar limits? You mentioned dispensing limits, but have you seen many plans that have a maximum amount for a quarter or for a year? Is that being done, and has that been effective?

MS. BERNACCHI: We see it frequently in Medicare plans and senior programs where because of the limited dollars available to spend on the total plan they will set limits on how many dollars you can get, either set per year or per quarter. That's where we see that most frequently.

MR. DOLSKY: My question is for all of you because you represent payers, PBMs and pharma. This transaction is so complicated. It was touched on briefly, but it's hard for many of us to figure out where the money is, where it's going, and who has how much. One of the buzzwords certainly in the industry is transparency. That is a future key direction of at least the PBM business. Could you comment on how far this transparency is going to go, if it's significant and if there's anything you have to say about why it's so complicated and hard to find the money?

MR. WILSON: Transparency is certainly the word in health care today. I don't know whether any of you attended the National Managed Health Care Congress in D.C. I did not attend, but the journal had one-page ads constantly, and every discussion was on transparency. To your point, Kevin, yes, we have made this as complex and as complicated as we possibly could.

In our defense on the PBM side, a lot of it was done at the suggestion of the payers and at the suggestion of third parties who would do some consulting work. I'm not pointing blame. I'm just pointing out history. Transparency can mean a number of things for a number of people, but there's also something called pass-through pricing. Now payers—predominately employers—are saying, "I want everything. I want 100 percent of the rebates. I want to be able to audit those rebates. I want to know that anything that you're getting in conjunction with this script I get." We'll say, "Fine. You want to look like a self-funded medical plan. Here's your administrative fee."

Someone from a consulting firm told me a funny story last week. A client hung up on him because he said, "We can get you pass-through pricing. We can get you 100 percent transparency. But you know that zero administrative fee you pay? That fee

is going to have to go up to a certain dollar amount on a per script basis." The employer said, "No. I want 100 percent pass-through, I want full transparency, and I want a zero administrative fee." He hung up on the consultant. We have some educating to do. The point is that it can be done, and we are doing it. It's certainly not the norm yet, but what we're finding is when clients start getting into it, they want to look at both. They want to look at the "traditional" with the rebate sharing and different revenue streams. They also want to look at transparency, and then they're making a decision. To be honest, more than half of the rebates go back to the employer or the payer. That's our perspective on it.

MS. WEAR: I would agree with what Chris just shared. The question comes back to what transparency means. Does it mean that the employers gets 100 percent of the rebates passed back to them, or is it that they feel as though they've gotten full disclosure on what the rebates are? Is it, as he's describing, the mix of what they keep for rebates and other monies that come in as compared to what the employers or health plans have to pay as an administrative fee to the PBM? I see it moving toward much more transparency. I don't know whether it is going to be full transparency.

MS. BERNACCHI: Our firm started out as an auditing firm. We audited PBMs on behalf of pharmaceutical manufacturers. Transparency's a problem for the pharmaceutical manufacturer side as well. Manufacturers paid $11 million rebates on a single invoice and had little access on audit even to what the PBM used to compile those invoices. Fraudulent fabricated claims came in from some PBMs, and the PBMs have cleaned up a lot in the past three or four years. If you go to any publicly traded PBM Web site under EDGAR under the SEC, you'll see that there are ERISA suits and there are suits from payer plans that allege that they are not getting what they think they should have been getting in terms of the rebate. These are complicated contracts. The rebates are not just a percentage of the cost of the unit sale that happened at the pharmacy. They are market shares. Complicated math goes into driving what the rebate was. Applying it to any given prescription or any given employer plan is a difficult thing to do.

Some legislation was passed in December that's going into effect next month on the Medicare program that requires specifically that there will be transparency down to the member level and that the Feds can and will audit the PBMs' rebates and other payments received by the pharmaceutical manufacturer in total down to the member level. I was at the National Council for Prescription Drug Programs (NCPDP) earlier this week. There are tremendous problems with regard to getting to that number and deriving it. As Chris said, the problem isn't necessarily that the PBMs are trying to get away with something, but that you're not paying the PBM for the services that it's rendering. The PBM or the payer then needs to find some way to cover that elsewhere. That's been done two ways: primarily through the pharmaceutical industry, but then also through network discounts and what they pay the retail pharmacy that isn't necessarily disclosed. The PBM industry is going to have to step up and hire people who will help them get to this transparency and

make sure that their systems get down to the level of the individual claim for the patient or for the plan.

MR. WILSON: I would just say one thing. There's so much activity over transparency. It amazes me that there's that much focus on a 2 percent margin business.

MS. BERNACCHI: They believe that it's bigger than 2 percent.

MR. WILSON: I know they do. I wish it were.

FROM THE FLOOR: The only comment I'll make about transparency is it's somewhat like the words "new," "improved" and "quality." That's another issue. I heard that in the first week or two after the discount cards went up on www.medicare.gov, there might have been a significant decrease in selling price. I'm wondering whether any of the panelists could comment on that.

MS. BERNACCHI: I've heard from a number of our clients that the prices that are out there are wrong.

MR. WILSON: The only thing I could add is ours showed as the lowest, and we thought it was great, but we're not sure how accurate they are either. We were talking at breakfast what it's going to mean when this goes live. I think a lot of people will be confused. They are confused already, but once they do it, they're going to be confused. I think there's going to be a lot of buyer remorse. I'm glad we're doing this early before '06, so hopefully we'll get some of these bugs out and offer a good benefit for these people.

MR. COREY N. BERGER: I don't know whether any of you are offering a discount card or have heard anecdotally about how many people have signed up. I haven't heard anything in the press as to whether it's 10 percent or 2 percent. Does anyone have any insights on that?

MR. WILSON: I don't. I have to disclose that you and I have a business relationship at a company level because we have worked with your parent company, UnitedHealthcare. We're cobranding with them. We sent out millions of pieces. I haven't received any feedback unless you have, Margaret.

MS. WEAR: We elected not to play in the stand-alone drug discount card market.

MS. BERNACCHI: One of the challenges from the pharmaceutical industry side of this is that there are the approved and endorsed programs. I don't know what the life count is on that. All you have to do is go into any corner drugstore. There are a lot of other discount programs that are one-offs for seniors that aren't necessarily endorsed programs, and I think that they are going to add to the confusion of the legitimate programs that are out there. Pharma is anticipating that it's going to

have to do a lot of vetting and validating the rebate submissions that are coming in from both legitimate and maybe not legitimate sponsors that are looking for rebate payment.

Chart1

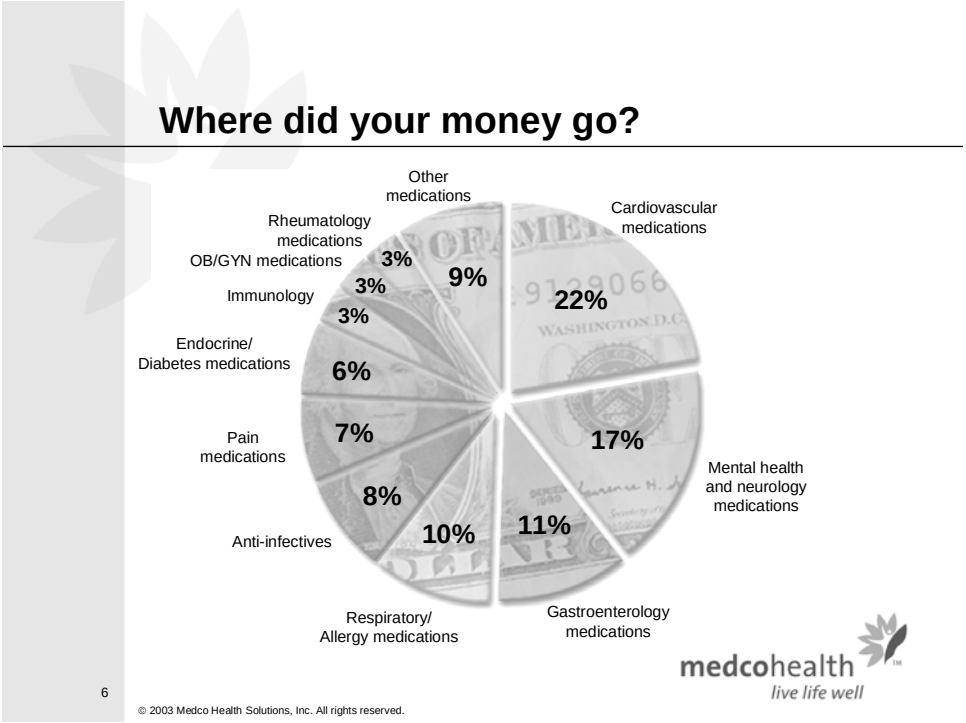
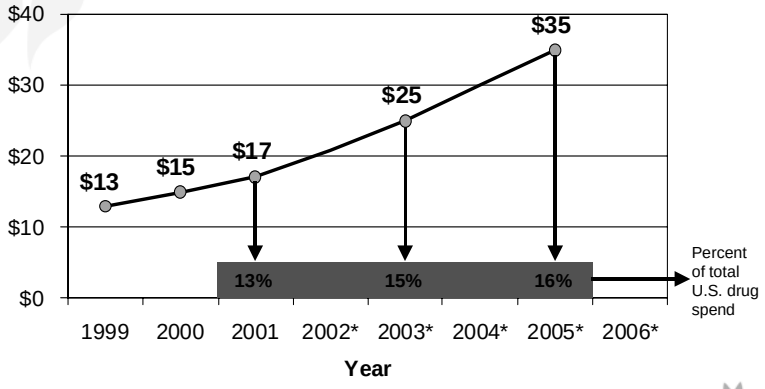


Chart 2

Specialty pharmacy growth is outpacing total prescription drug spend

($ billions)



* Projected
Source: Lehman Brothers report, CMS

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Chart 3

Specialty pharmacy drugs on the horizon 2003-2005

Disease state	U.S. population affected	Drugs under investigation	Estimated sales
Acromegaly	? 11,000-15,000	pegvisomant (Somavert)	$150 million
Asthma	? 17 million total ? 7.7 million have the allergic form ? 4.6 million have high IgE levels	omalizumab (Xolair)	$750 million
Cancer	>7 million	erlotinib (Tarceva) jefitinib (Iressa) rubitecan (Orathecin) tipifarnib (Zarnestra)	$600 million $250 million No data available No data available
Crohn's disease	? 500,000	natalizumab (Antegren) CDP 571 (Humicade)	$400 million $100 million
HIV/AIDS	? 900,000	enfuvirtide (Fuzeon)	$500 million
Psoriasis	? 4.5-5.5 million total ? 1.5 million have moderate to severe disease	efalizumab (Raptiva) etanercept (Enbrel) adalimumab (Humira) infliximab (Remicade)	$1 billion $1 billion $600 million No data available
Pulmonary hypertension	? 2,000-5,000	beraprost (none) iloprost (none)	No data available No data available
Rheumatoid arthritis	? 2.1 million	CDP 870 (none) interleukin-10 (Tenovil)	$500 million $250 million

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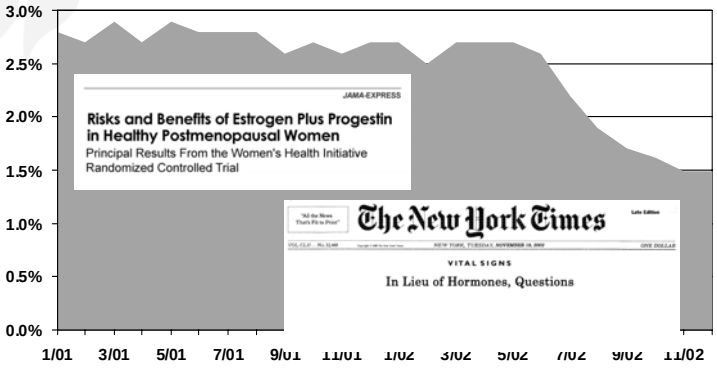
Chart 4

New clinical findings impact utilization

Percentage of women filling a prescription for HRT

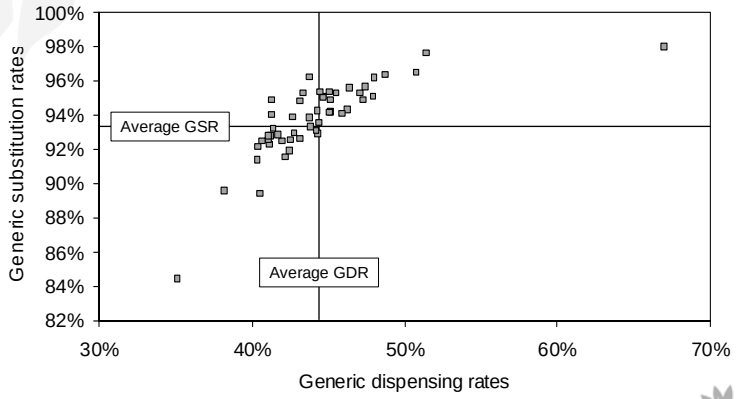


Source: Medco Health data

Chart 5

Patent expirations provide opportunities for cost savings

Generic rates vary by state

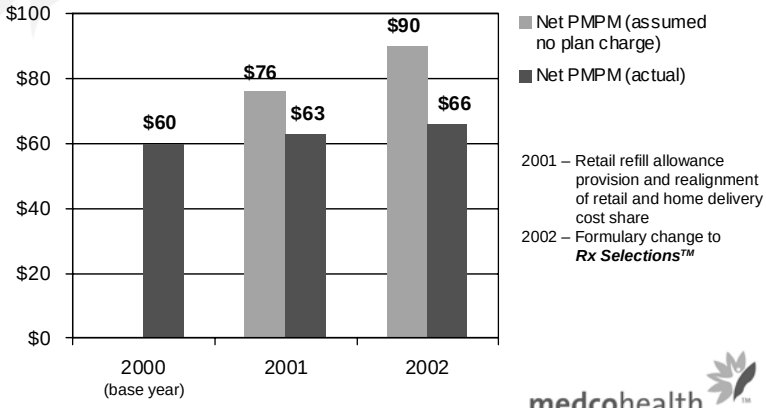


Source: Medco Health data

Chart 6

Case study

Ongoing plan management lowers per member per month (PMPM) costs



Source: An employer in the energy industry; 100,000 lives

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