

# **Controlling Pharmaceutical Costs The Evolving PBM Model**

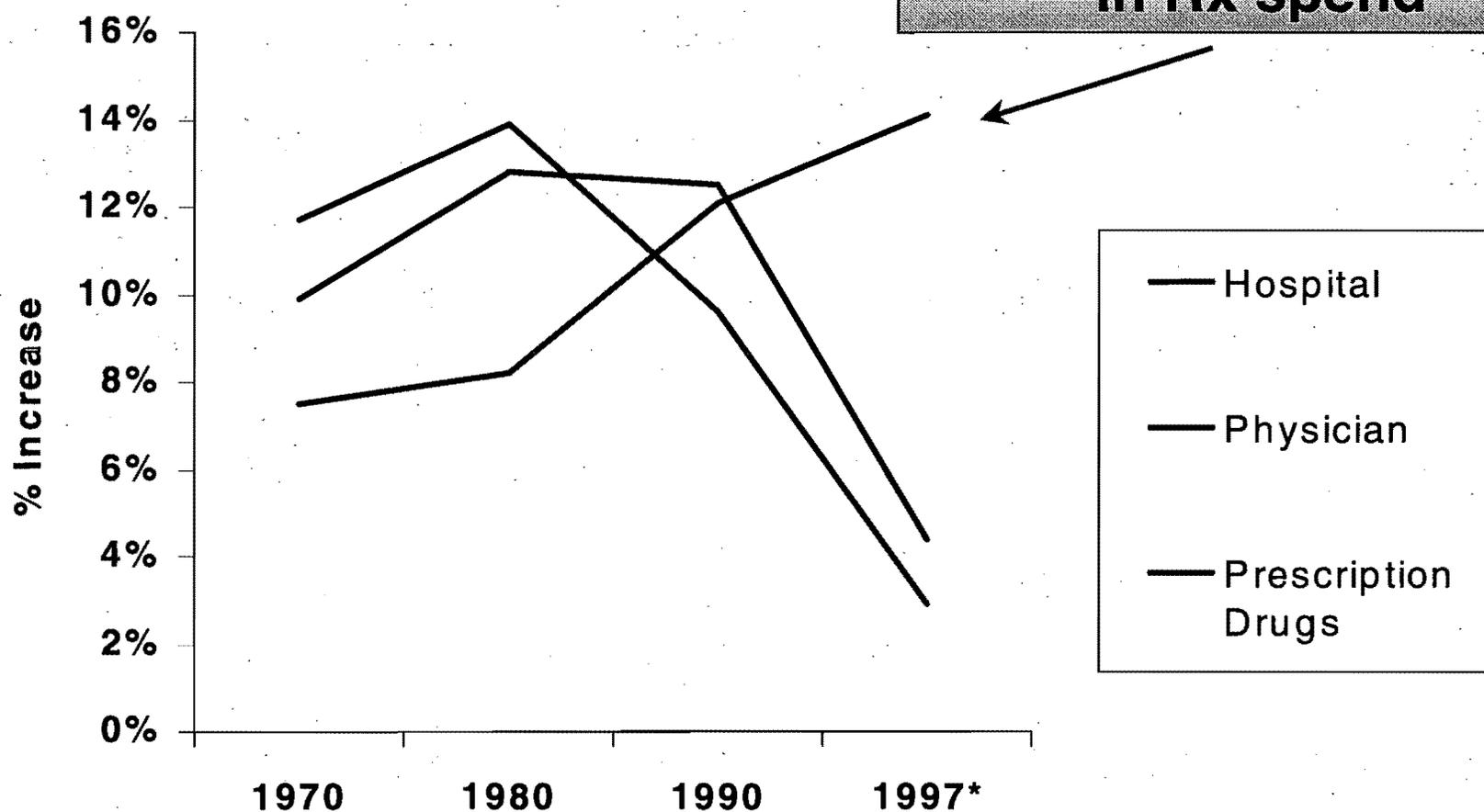
**Elizabeth Dichter  
Executive Vice President  
PCS Health Systems, Inc.**

**October 1999**

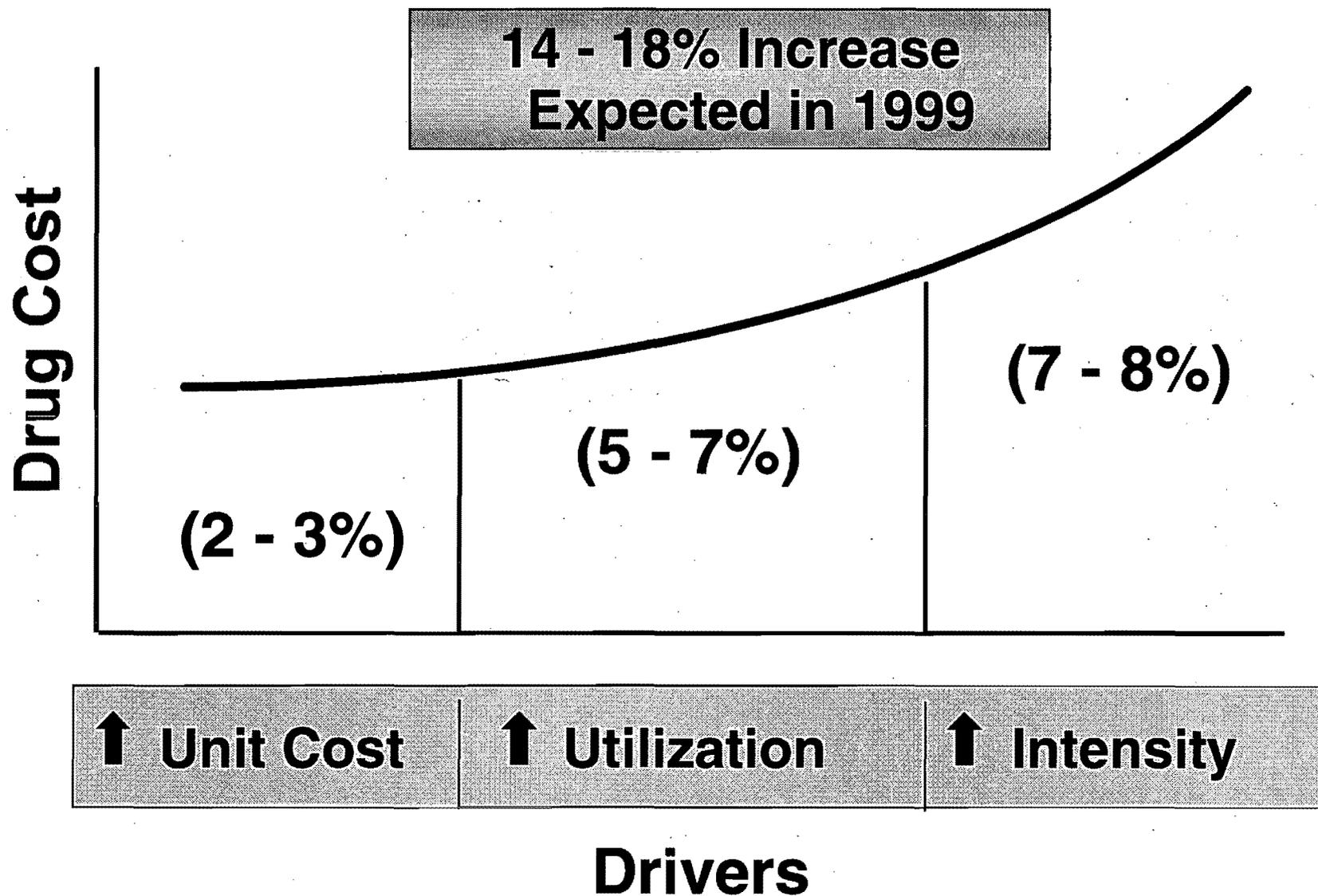


# Why The Focus On Drugs?

## U.S. Healthcare Expenditures



# Drug Spend Drivers



Source: PCS Analysis

# Industry Tension

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## PHARMACEUTICAL COMPANIES

## MANAGED CARE ORGANIZATIONS

**Capitalization:**

\$830 billion

\$36 billion

**PE Ratio:**

37

18

**1998 Profit:**

\$20 *billion*

\$290 *million*

**R&D:**

14% of sales

Is it affordable?

**Value Base:**

Intellectual capital

Cost containment

**Rewarded On:**

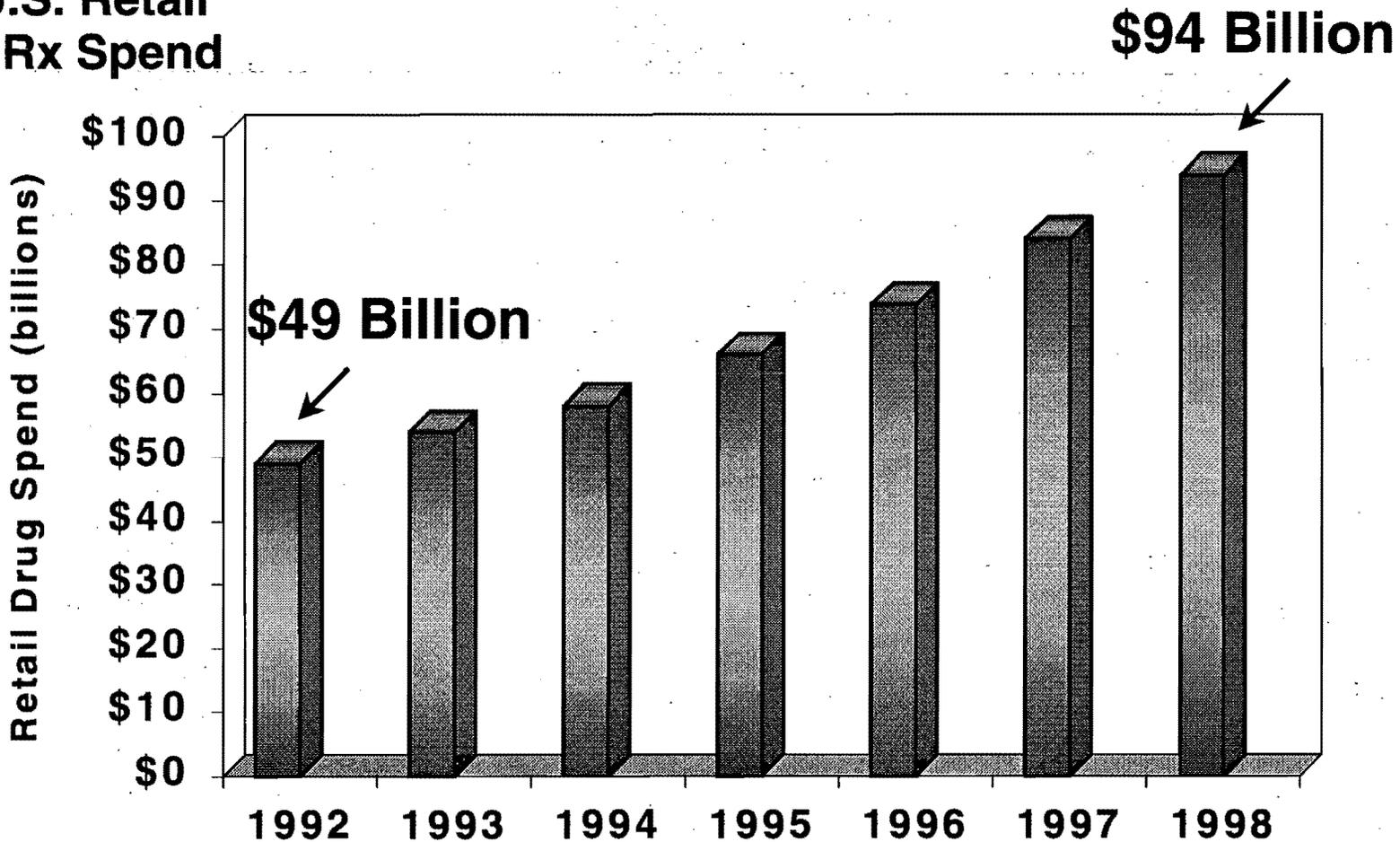
Cure diseases

Manage budgets



# What the Payer Sees

## U.S. Retail Rx Spend



# Why More Drugs Now?

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## Consumer Price Inelasticity

- 3rd party coverage
- Flat, low copays

## Aging Population

- ↑ life expectancy
- 1m new 65 yr olds / year
- 35% of all Rx spend

## Pharmaceutical Marketing

- 48% sales force ↑ in past three years
- Direct-to-consumer advertising: 120% ↑ in two years

## New Drugs, New Protocols

- Rich product pipelines
- Doubling of new drug approvals
- New diabetes treatment standards



*What Could Change the Curve?*

# The Cost of New Technologies

<u>New Drug</u>		<u>Predecessor</u>	
SSRI (Prozac)	\$2.36	amitriptyline	\$0.17
Lipitor	\$1.80	gemfibrozil	\$1.04
Prilosec	\$3.59	cimetidine	\$1.60
Celebrex	\$2.42	NSAIDs	\$1.20
Rezulin	\$2.98	glucophage	\$1.90
Claritin	\$1.23	chlorpheniramine	\$0.96
Viagra	\$8.75	yohimbine	\$0.50



## What Could Change the Curve?

# New Product Development

	<b>1998</b>	<b>1999</b>	<b>2000</b>	<b>2001</b>
<b>Cardio</b>	Avapro Atacand	Teveten	Imidapril Cardura*, Vasotec*, Cozaar*	Prinvil* Zestril* Mevacor*
<b>Central Nervous</b>	Reductil Maxalt	Exelon Memric Relpax Edronax Klonpin*	Tamoxetine BuSpar* Neurontin*	MK-869
<b>Diabetes</b>	Prandin	Avandia, Actos Glucophage*	A-4166	Inhaled Insulins
<b>Respiratory (Asthma)</b>	Singulair Atrovent*	Ultair Beclovent*	Asmanex	
<b>Arthritis/ Chronic Pain</b>	Enbrel Arava	Celebrex Vioxx	Mobic	MK-663
<b>Women's Health</b>	Evista	droloxifene idoxifene	Actonel levormeloxifene	

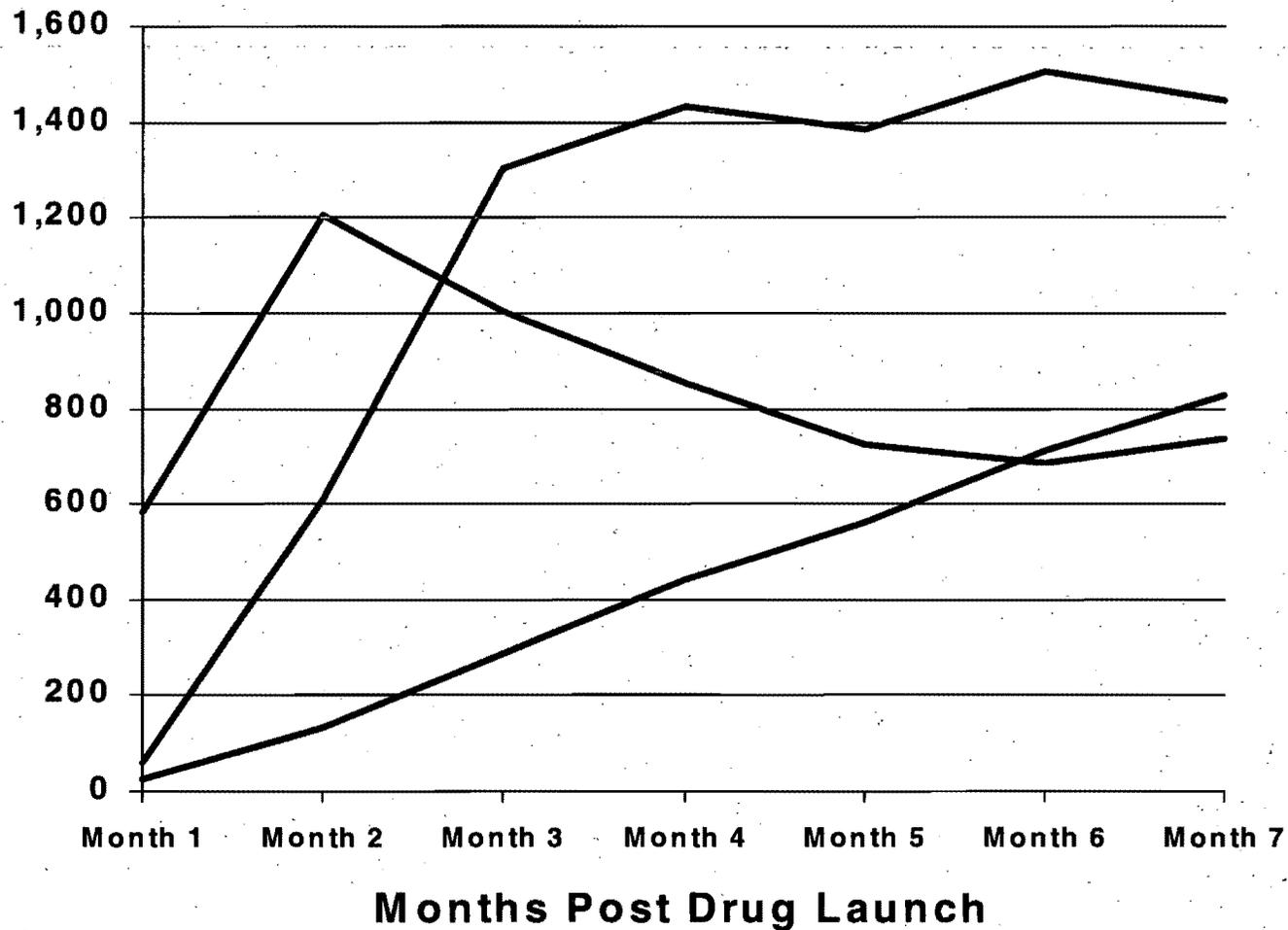
Drug names in pink and noted with an asterisk (\*), represent drugs with patent expirations.

Sources: Various analyst reports and industry literature; NOTE: Drug launches listed in table are best estimates based on current information.



# Industry Watch: Pain

## Monthly U.S. Retail Prescriptions (Rx in Thousands)



**Celebrex**  
(Launched 1/99)

**Lipitor**  
(Launched 1/97)

**Viagra**  
(Launched 4/98)



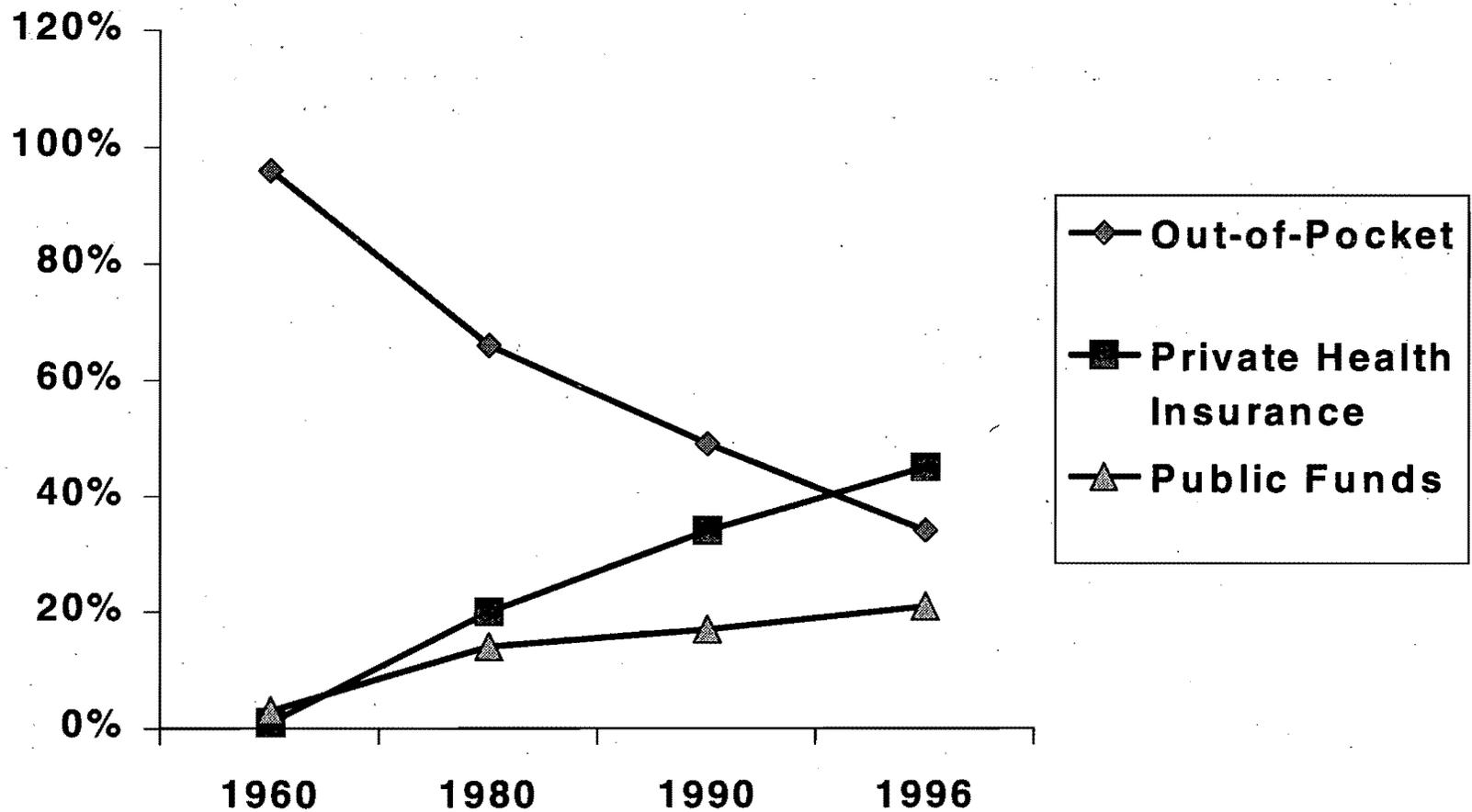
*What Could Change the Curve?*

# **Growth of Legislative Initiatives**

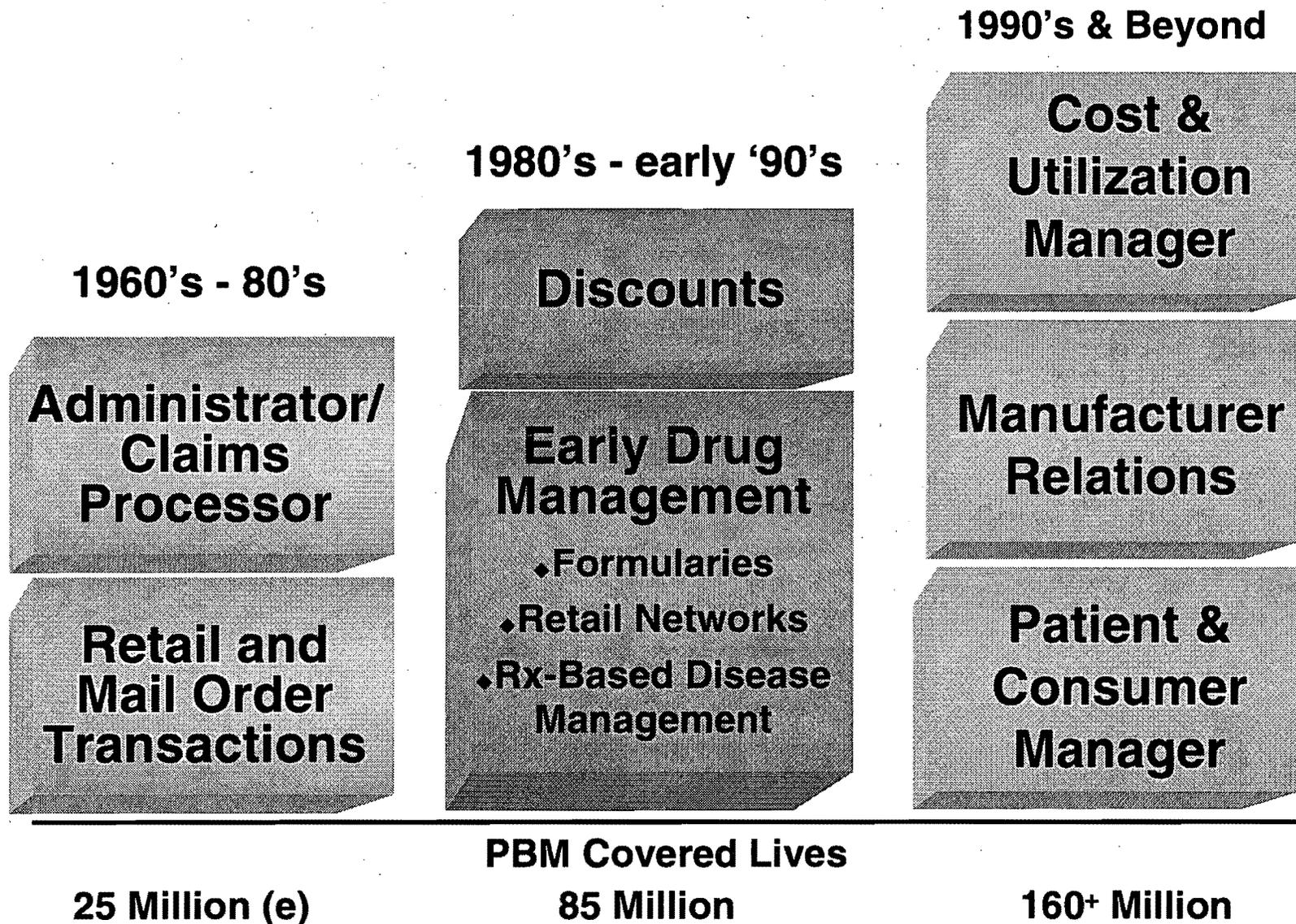
- Demand for Choices
  - More benefits security
  - More flexibility and plan coverage
- Access to Information
  - Focus on quality
  - Detailed reporting; key source = Internet
- Legislative Initiatives
  - Patient “Bill of Rights”
  - “Length of Stay” Legislation
  - Enterprise Liability



# Who Will Pay? Client vs Member Share



# Evolution of PBMs



# Intelligent Drug Management

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## Plan Design

- ◆ Deductibles, Copayments, Coinsurance
- ◆ Drug Coverage (Life Saving vs Life Style)

## Plan Management

- ◆ Member Eligibility
- ◆ Member - Physician - Pharmacy Education
- ◆ On-Line, Real Time Claims Adjudication

## Formulary Management

- ◆ Preferred Drug List
- ◆ Optimizing Manufacturer Opportunities



# Intelligent Drug Management

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## Pharmacy Management

- ◆ Network Options (Retail, Mail Order)
- ◆ Network Design (Open, Custom)
- ◆ Network Performance & Incentives

## Utilization Management

- ◆ Drug Utilization Review (DUR)
- ◆ Dispensing Limits, Prior Authorizations
- ◆ Compliance Programs

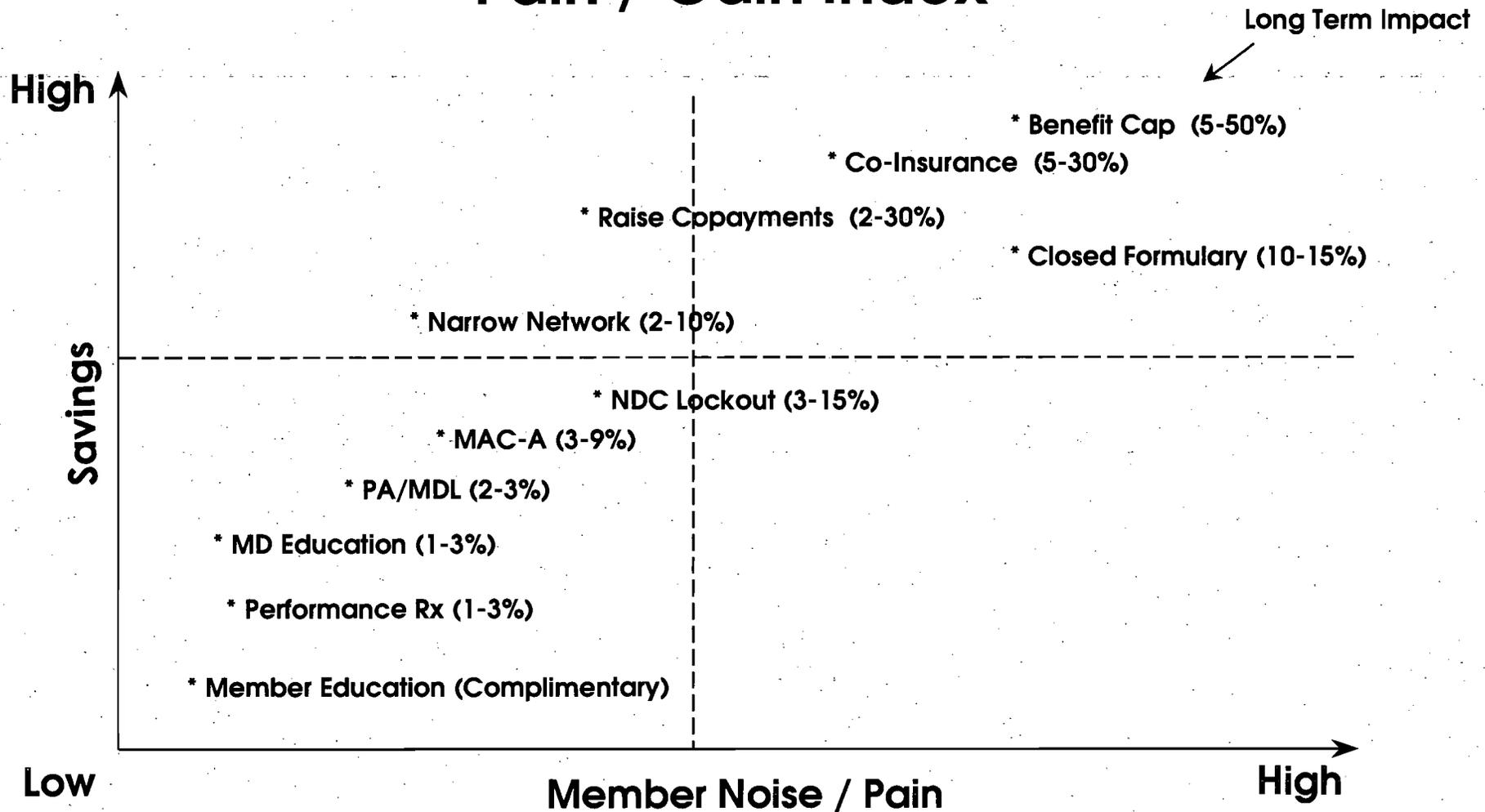
## Merging Medical & Drug Information

- ◆ Disease Management Programs
- ◆ High Risk and High Cost Populations
- ◆ Case Management



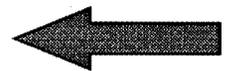
# Trading Cost Savings with Member Impact

## Pain / Gain Index

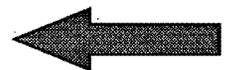


# HMO Trends in Formulary Cost Controls

	<b>1996</b>	<b>1997</b>	<b>1998(e)</b>	<b>1999(e)</b>
<b>Generic Substitution</b>	<b>95.5%</b>	<b>97.7%</b>	<b>95.5%</b>	<b>93.2%</b>
<b>Prior Authorization</b>	<b>81.8%</b>	<b>90.9%</b>	<b>93.2%</b>	<b>90.9%</b>
<b>Preferred Status</b>	<b>63.6%</b>	<b>75.0%</b>	<b>77.3%</b>	<b>75.0%</b>
<b>Therapeutic Interchange</b>	<b>31.8%</b>	<b>47.7%</b>	<b>54.5%</b>	<b>61.4%</b>
<b>Restricted Use</b>	<b>59.1%</b>	<b>65.9%</b>	<b>65.9%</b>	<b>63.6%</b>
<b>Variable Copayments</b>	<b>52.3%</b>	<b>63.6%</b>	<b>81.8%</b>	<b>86.4%</b>



**Significant  
Increases**



# PCS Savings Example: Three Tier Copay Plan Design

Old Design: \$5 Generic / \$10 Brand Copay Plan

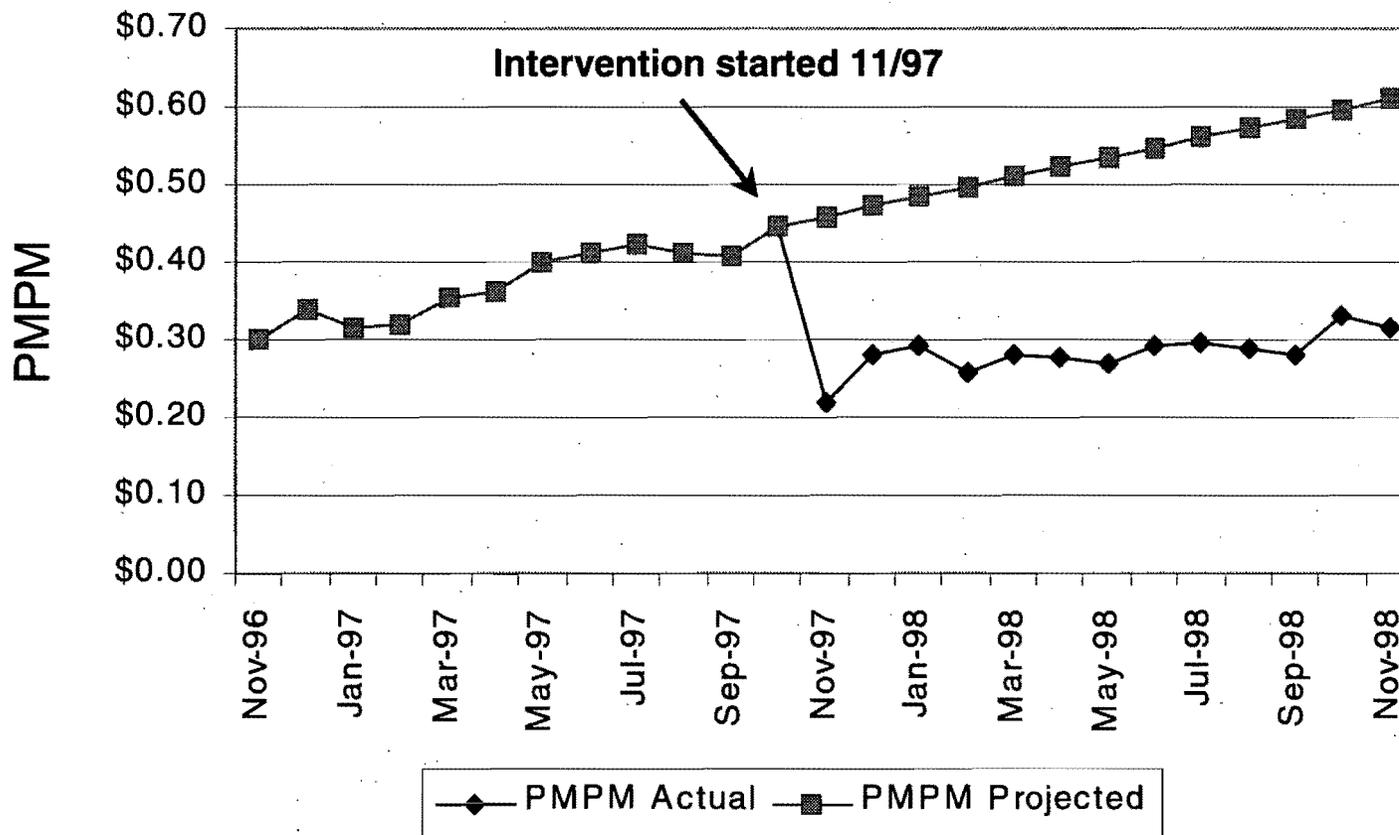
	New Three-Tier Design	
	Design 1 <u>\$5/\$10/\$20</u>	Design 2 <u>\$5/\$10/\$30</u>
Drug Cost Savings	2-4%	3-5%
Cost Share Savings	4-5%	8-9%
Total Savings*	6-9%	11-14%

\*Final savings will vary based on drug mix, generic policy, geographic area and other factors



# PCS Savings Example: Managed Drug Limitation on Imitrex

- Amount paid decreased 33%
- Quantity per member decreased by 32% for oral meds and by 45% for injectables
- Quantity per Rx decreased by 25% for oral meds and by 30% for injectables



# Pharmacy Substitution and Interchanges

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	<u>Gen. Sub Rate</u>	<u>Gen. Disp. Rate</u>	<u>Ther. Int. Success Rate</u>
<b>WalMart</b>	<b>87%</b>	<b>43%</b>	<b>18%</b>
<b>Rite Aid</b>	<b>89%</b>	<b>46%</b>	<b>30%</b>
<b>CVS</b>	<b>84%</b>	<b>40%</b>	<b>16%</b>
<b>Eckerd</b>	<b>85%</b>	<b>41%</b>	<b>15%</b>
<b>Walgreen</b>	<b>86%</b>	<b>42%</b>	<b>0%</b>
<b>Independents</b>	<b>82%</b>	<b>40%</b>	<b>17%</b>
<b>All PCS</b>	<b>84%</b>	<b>41%</b>	<b>18%</b>



*What Could Change the Curve?*

# Coverage Limitations

- Increased Use of Restrictions
  - Viagra
  - Standard of 6 pills per month
  - Celebrex
    - Restricted use (Wellpoint, Aetna)
    - Low reimbursement level (UHC, Kaiser)
- Aligning Financial Responsibility
  - Three Tier Co-Payment Structures
    - \$5 to \$5 / \$10 to \$5 / \$10 / \$25
- Decreasing Popularity of Closed Formulary



# Precursors to Success

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- **Align Incentives for Healthcare Delivery**
  - Medical, Rx, Diagnostic Coverage
  - Adoption of Standards of Care
- **Consumer Education**
  - Awareness + Knowledge = Decision Maker
  - Behavioral Compliance
- **Availability and Integration of Data**
  - Rational Patient Confidentiality Policy
  - Patient Centric Focus



# Obstacles to Success

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- **Fragmentation of ...**

- Healthcare Data
- Delivery Systems
- Population Demographics

- **Rational Decisions on ...**

- Incentives for Integration of Patient Care (e.g., preventive care)
- Who Pays for What
- Patient / Data Confidentiality



# Developing a Drug Management Strategy

- Evaluate your medical and prescription drug needs: demographics
- Understand the Rx environment
  - Products, marketing efforts, future promises
- Understand the performance of your delivery system
  - Pharmacies, MD's, etc.
- Determine what and how much you can control
- Determine what you are willing to do



# Payer Strategies

- Increased cost sharing
  - ◆ Generic - Preferred Brand - Brand
- Elimination of coverage for “discretionary” or “cosmetic” products
- Narrower formularies and pharmacy networks
- Advanced Rx management tools
  - ◆ Prior Authorization
  - ◆ Managed Drug Limitation
  - ◆ Refill-Too-Soon
- Increased manufacturer rebates, risk sharing and financial support



# Who Will Pay for What?

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## Life Saving

- Antibiotics
- Cancer treatments
- Asthma
- Diabetes



## Life Enhancing/Lengthening

- High cholesterol
- High blood pressure
- Allergies
- Depression
- Migraine
- Arthritis
- Obesity



## Life Style

- Fertility
- Sexual dysfunction



## Cosmetic

- Wrinkles
- Baldness
- Short stature



PPI - Pharmaceutical Preparations, NSA  
 COMMODITY WEIGHTED - CC 0635  
 1982 = 100

Month	0635 Index	Twelve Month Change
Dec-96	267.9	2.0%
Jan-97	270.2	3.0%
Feb-97	271.0	3.4%
Mar-97	271.9	3.3%
Apr-97	271.6	3.1%
May-97	272.7	2.7%
Jun-97	273.2	2.6%
Jul-97	273.4	2.4%
Aug-97	273.5	2.5%
Sep-97	273.9	2.8%
Oct-97	275.7	3.4%
Nov-97	277.1	3.9%
Dec-97	277.5	3.6%
Jan-98	278.4	3.0%
Feb-98	282.7	4.3%
Mar-98	284.1	4.5%
Apr-98	287.9	6.0%
May-98	319.3	17.1%
Jun-98	328.8	20.4%

Note: PPI is  
 subject to  
 4 month revision

PPI - Pharmaceutical Preparations  
 INDUSTRY WEIGHTED - SIC 2834 #1  
 06/81 = 100

Month	2834 1 Index	Twelve Month Change
Dec-96	302.1	2.1%
Jan-97	304.6	3.0%
Feb-97	305.7	3.4%
Mar-97	306.7	3.4%
Apr-97	306.3	3.1%
May-97	307.5	2.7%
Jun-97	308.1	2.6%
Jul-97	308.4	2.4%
Aug-97	308.4	2.5%
Sep-97	308.9	2.8%
Oct-97	311.0	3.4%
Nov-97	312.5	3.9%
Dec-97	313.0	3.6%
Jan-98	313.9	3.1%
Feb-98	318.9	4.3%
Mar-98	320.5	4.5%
Apr-98	324.7	6.0%
May-98	360.4	17.2%
Jun-98	371.3	20.5%

All Finished Goods, NSA  
 1982 = 100

Month	All Finished Index	Twelve Month Change
Dec-96	132.7	2.8%
Jan-97	132.6	2.5%
Feb-97	132.2	2.2%
Mar-97	132.1	1.5%
Apr-97	131.6	0.8%
May-97	131.6	0.4%
Jun-97	131.6	-0.1%
Jul-97	131.3	-0.2%
Aug-97	131.7	-0.2%
Sep-97	131.8	0.0%
Oct-97	132.3	-0.3%
Nov-97	131.7	-0.7%
Dec-97	131.1	-1.2%
Jan-98	130.3	-1.7%
Feb-98	130.2	-1.5%
Mar-98	129.7	-1.8%
Apr-98	130.0	-1.2%
May-98	130.4	-0.9%
Jun-98	130.6	-0.8%

Medicare Reim: Wyden / Source Re. Pay File



U.S. Senator Ron Wyden



FAX TRANSMISSION

516 Hart Senate Office Building  
Washington, D.C. 20510  
(202) 224-5244  
(202) 228-2717 (Fax)

URGENT

Date: 10/22/99

To: ~~BRUCE~~ DEVORAH

Fax: 6-5557

From: BRUCE

Subject: INFO on PRESCRIPTION  
DRUGS BILL

Pages: 2  
(Including cover)

COMMENTS:

call me

pls save  
backup  
information  
for info w/  
Ron Wyden

News Advisory . . .

# U.S. Senators Ron Wyden & Olympia Snowe

FOR IMMEDIATE RELEASE  
September 24, 1999

Contacts: Lisa Finkel (Wyden), 202/224-5244  
Dave Lackey (Snowe), 202/224-5344

## WYDEN, SNOWE TO LAUNCH GRASSROOTS CAMPAIGN FOR PRESCRIPTION DRUG COVERAGE

*Senators Take to the Senate Floor to Urge Seniors to Send in Their Bills*

Washington, DC – U.S. Senators Ron Wyden (D-Ore.) and Olympia Snowe (R-Me.) will address the U.S. Senate to launch their grassroots campaign for prescription drug coverage on Tuesday, September 28.

Snowe and Wyden are the authors of the Seniors Prescription Insurance Coverage Equity (SPICE) Act -- the *only* bipartisan bill to provide prescription drug benefits to all Medicare recipients.

Wyden and Snowe, who earlier this year won 54 votes in the Senate for a budget amendment to direct tobacco tax revenues toward a prescription drug benefit, will discuss their legislation and urge seniors to send copies of their prescription drug bills to their Senators to draw attention to the cause.

Wyden and Snowe's remarks will be broadcast on C-SPAN 2. The coordinates are Sat Com C-4; Transponder 19.

- WHO: U.S. Senator Ron Wyden (D-Ore.)  
U.S. Senator Olympia Snowe (R-Maine)
- WHAT: Sens. to Launch Grassroots Prescription Drug Coverage Campaign  
Bipartisan Duo to Urge Seniors to Send in Their Bills
- WHEN: Tuesday, September 28, 1999
- TIME: TBD  
(All times are subject to changes in the legislative schedule.)
- WHERE: Senate Floor, The Capitol  
###

Wyden and I have been united in the belief that we owe it to seniors to develop the best and most practical solution. SPICE represents a straightforward, comprehensive, and responsible approach that should appeal to anyone who agrees that seniors need coverage of prescription drugs.

"Cynics are asking, 'Can the country afford to cover prescription drugs?'. I believe we can't afford not to. It's not pie-in-the-sky, but a reasonable idea that actually provides coverage for needy seniors through a delivery system that's senior-friendly and uses marketplace competition and consumer choice to hold down costs," Wyden said.

Snowe and Wyden said that their approach offers an "affordable, realistic" approach to covering prescription drug costs, and said they would rely for funding on the 55 cent increase in tobacco taxes, and acceleration of a 15-cent increase already in law, as proposed in President Clinton's budget. A special reserve fund for prescription drugs, created during Senate consideration of the Fiscal 2000 Budget Resolution through an amendment offered by Snowe and Wyden, will provide a portion of the \$505 billion from the non-Social Security on-budget surplus if necessary, they said. The budget reserve fund is triggered if the Senate Finance Committee reports legislation significantly extending the solvency of the Medicare program.

Under the Snowe-Wyden SPICE Act, beneficiaries will choose among comprehensive coverage options for their prescription drug needs under guidelines set and approved by an independent board. The board will establish a model plan, and a cap on out-of-pocket spending for prescription drug expenses, and beneficiaries will be responsible for a co-pay and annual deductibles. The benefit will be administered by an independent agency, reporting to the Secretary of Health and Human Services.

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### SENIOR PRESCRIPTION INSURANCE COVERAGE EQUITY (SPICE) ACT Senators Olympia Snowe and Ron Wyden

**Eligibility:** All seniors who are eligible for Medicare Parts A and B will be eligible for a SPICE drug plan. Seniors will choose from competing benefit plans, which will pay for prescription drug costs with varying deductibles and copays. In this way, seniors may choose the plan that best fits their needs.

**Financial Assistance:** Seniors earning below 150 percent of the poverty level ( currently \$12,075/ single, \$16275/couple) will pay no premiums for prescription drug insurance plan of their choice. For those earning between 150 percent of poverty and 175 percent (\$14088/single, \$18988/couple) will have their premium assistance phased down from 100 percent to 25 percent. All other seniors will have 25 percent of their premiums subsidized. The policies will all meet a threshold standard developed by the SPICE.

**Plan Options:** The SPICE Board would work with the National Association of Insurance Commissioners to develop the threshold drug benefit using the FEHBP program and large group market plans as a guide. Plans would then compete to offer plans at either the threshold level or better so seniors could have a choice of plans. NAIC will also make recommendations to the SPICE Board concerning offering a drug plus other benefits policy through SPICE.

In addition, beneficiaries in Medicare +Choice plans that charge premiums for a drug benefit would receive some assistance.

**Administration:** The program would be administered by the SPICE Board that would be separate from the Health Care Financing Administration, but report to the Secretary of HHS. The Board would provide information, make sure consumers have choice of plans, and report to Congress concerning the funding and benefit design adequacy for seniors health care needs.

Plans would have to be approved at the state level just like current medigap policies is currently, and by the SPICE Board. Consumer protections that apply to medigap would apply to these plans.

An open annual enrollment would be available so seniors could change plans or get coverage should their Medicare+choice plan or private prescription drug plan terminate.

**Financing:** SPICE will be funding through the on-Budget, non-Social Security surplus and a 55 cent tobacco tax increase and acceleration of a 15 cent increase in tobacco taxes already in law.

## Seniors Prescription Insurance Coverage Equity Act Senator Olympia Snowe/ Senator Ron Wyden

The SPICE Act creates a voluntary supplemental drug insurance policy that all Medicare eligible individuals can purchase. These policies will be guaranteed issue -- no one can be turned down. SPICE eligibility will begin when Medicare eligibility begins. There will be a penalty for late entry, just as there is for those who make a late entry into the Medicare Part B program. The penalty fee for late entry will be waived if the late entry is based on the loss of prior drug coverage from a Medicare + Choice plan or a retiree group health plan.

All seniors will receive some premium support assistance on a sliding scale based on income. Every senior will receive at least 25% premium support. Those below 150% of the federal poverty line will receive 100% premium support. A sliding scale will phase down the premium support from 100% to 25% for those between 150% and 175% of the federal poverty line.

The federal premium support will be used to allow seniors to purchase SPICE policies from private providers, similar to the Medigap program. The policies will all meet a threshold standard developed by the SPICE Board, which includes consumers, state insurance commissioners, and insurance representatives, and will be designed with seniors needs in mind. Medicare+Choice and group health plans which provide drug coverage for Medicare eligible individuals will be able to receive the actuarial value of the drug benefit if their plans meet or exceed the SPICE Board threshold benefit plan.

Seniors will be given a choice of plans. This will ensure competition and help keep the costs down and will allow seniors to choose the plan that best meets their needs. To provide an idea of the types of choices, plans may offer coverage for different drugs (formularies), copays, deductibles, and caps. The SPICE Board will disseminate information about these choices, much like the Federal Employee Benefit Health Program (FEHBP) does.

Funding sources for the benefit will come from the on-budget surplus, which the Congressional Budget Office (CBO) estimates show to be \$505 billion after the \$792 billion tax cut legislation that is currently in conference. Additional funding may come from implementing the President's FY2000 budget proposal to raise the tobacco tax by 55 cents per pack in addition to enacting the 15 cent tobacco increase already in law one year earlier than originally planned.

[pS10222]

Mr. WYDEN. Mr. President, today Senator SNOWE and I are introducing legislation to provide seniors with insurance coverage for prescription drugs. This legislation, the Seniors Prescription Insurance Coverage Equity Act, SPICE, is the only bipartisan, market-based approach to provide seniors with choice and access to coverage that is actually paid for. It will give seniors the same kind of coverage that their member of Congress has.

The key issue for seniors around our nation, when it comes to the issue of prescription drugs, is affordability. Our proposal will assure that each and every senior who voluntarily chooses to enroll in a SPICE plan will have the bargaining power of HMOs and of the large insurers whose job it is to get the best price they can. At least 13 million seniors have no prescription drug coverage at all. Those seniors get penalized twice: they have to pay all their costs, and they pay more because they can't get the negotiated rate that the insurers and HMOs can. This bill will level the playing field for those seniors giving them affordability and access.

We know the kinds of drugs that are coming on the market now can help save lives, better the health status of an older person and, in many instances, save dollars because seniors taking their prescription drugs as they are told to by their doctor will prevent costly hospitalizations and the progression of disease. If we were to create Medicare today from scratch, there would be no questions about including prescription drug coverage. If we want to assure that Medicare beneficiaries stay healthy longer we must provide prescription drug coverage. If we want to be thoughtful, prudent purchasers of health care, we must find a way to assure seniors access to the drugs.

I believe the Snowe-Wyden proposal is that thoughtful, prudent and reasonable way. It assures a variety of options for coverage, and it assures that we bring real dollars to the table to pay for the program. There is no smoke and mirrors, no IOUs or other budget gimmicks in this plan.

The Snowe-Wyden proposal will be funded by funding from the non-Social Security on-budget surplus and a 55-cent increase in the tobacco tax. During this body's deliberations of the budget resolution, an amendment that Sen. SNOWE and I offered received 54 votes, including 12 Republican votes to do just this-fund a prescription drug benefit for seniors with an increase in the tobacco tax.

The SPICE legislation creates a senior-oriented program using the Federal Employees Benefit Program (FEHBP) as a model to provide benefits that

include prescription drugs and other non-Medicare covered benefits. This benefit would be open to every beneficiary and be voluntary. However, if the senior elected coverage later rather than when they were first eligible, the individual would pay incrementally more the longer he or she waited to choose a comprehensive coverage option.

The individual senior would be able to select from an array of drug policies and Medicare-Choice plans with prescription drugs coverage. This would be voluntary. No senior would have to change what their current coverage is if they do not choose to do so. All plans would be offered by private sector companies. For beneficiaries under 150 percent of the poverty level—\$12,075 for a single senior and \$16,275 for a couple, the federal government would pay the entire premium. For those between 150 percent and 175 percent of the federal poverty level, the amount the federal government would pay phases down from 100 percent of premium to 25 percent of the premium amount. For beneficiaries at 175 percent of poverty and over, the federal government would pay 25 percent of the premium amount.

Our SPICE benefit will be administered by a new Board that would be separate from the Health Care Financing Administration but report to the Secretary of Health and Human Services. The Board would approve plan designs and premium submissions, approve and distribute consumer education materials, develop enrollment procedures and make recommendations concerning additional funding, further ability to pay mechanisms and other steps needed to assure continuing availability of comprehensive coverage as seniors' health needs change over time.

Many of us would prefer to do an overhaul of Medicare and modernize it to include benefits like prescription drugs. However, the thirteen million Medicare beneficiaries who need coverage and the millions who have coverage that does not truly help them, need a way to get meaningful coverage today. This proposal will do that.

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Source: Government Printing Office

[Redacted text block]

[Redacted text block]

Chris -

Tony asked me  
to send you a  
copy of his memo  
to you.

Thank you.

Judy Butler

**MEMORANDUM**

**DATE: 10/7/99**  
**TO: CHRIS JENNINGS**  
**FROM: TONY PODESTA**  
**RE: ORPHAN DRUG ACT - EVERGREENING**

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I am writing to follow up on our discussions about "evergreening" of exclusivity periods under the Orphan Drug Act. As we discussed, it now appears that ODA exclusivity periods can be extended into infinity by multiple, overlapping applications. There is no evidence that Congress intended exclusivity periods beyond the initial seven years. The FDA should be mindful of the best interests of patients in interpreting the statute.

One class of patients suffering from the FDA's decision to allow overlapping exclusivity periods is MS victims. A story in the June 8, 1999 *New York Times* entitled "Experts Ask Why So Few Take Drugs for M.S.," cited a study that showed that "only 18% of the people who could benefit from the drugs were using them". And one of the cruel ironies associated with this disease is that patients who need therapies most (because their symptoms are so severe) are the most likely to be discouraged!

Serono Labs manufactures a drug called Rebif that is easier to administer (because it's available in pre-filled syringes) and is safe at higher dosage levels. Despite its considerable benefits, Rebif is not available to patients in the U.S. Betaseron and then Avonex were granted exclusivity under the Orphan Drug Act (ODA), creating a ten year exclusivity barrier to new entrants. Our meetings with staffers like Joel Johnson, who were present at the creation, have demonstrated that the authors of ODA did not intend to create evergreening situations, where new therapies are barred during overlapping exclusivity periods.

I believe it makes no sense to allow evergreening to bar beneficial drugs from reaching MS patients. If you would call Jane Henney and express your views, you would be performing a service for thousands of MS patients.

Thank you for your attention to this issue; please let me know if you need any additional material.

## Beta Interferon Drugs for Multiple Sclerosis

### SCOPE AND DURATION OF ORPHAN DRUG EXCLUSIVITY

Prior to 1993 FDA designated two beta-interferon drugs – Betaseron and Avonex - as orphan drugs for treatment of relapsing remitting multiple sclerosis, a disease which met the statutory test of an orphan since it affected fewer than 200,000 persons in the U.S.

Betaseron was approved in 1993 and by law became entitled to seven years of marketing exclusivity. No other beta-interferon could be approved for relapsing remitting MS unless it demonstrated "clinical superiority" to Betaseron.

In 1996 the second drug, Avonex, was allowed onto the market despite the Betaseron exclusivity because as a once per week intramuscular injection it was discovered to cause fewer injection site reactions in MS patients than Betaseron, which requires subcutaneous injections every other day. FDA regarded Avonex as "clinically superior," a regulatory concept FDA uses to determine whether two drugs are the same or different for orphan drug purposes.

A third drug, Serono's Rebif, was tested in two dosage strengths, each administered subcutaneously three times per week. FDA rejected Serono's argument that, assuming safety and efficacy is proved, its higher dose should be considered clinically superior to the two other drugs based on the Rebif study findings alone. The Serono drug now awaits final approval, which should occur in December. However FDA says it will not regard it as clinically superior without head to head evidence. Therefore, Rebif will be withheld from the market until expiration of exclusivity for both the first and second drugs, i.e. May 2003.

In March of this year Serono asked FDA to decide, as a matter of policy, that competition for the first drug should be allowed when its exclusivity expires next year. The second drug, assuming it is entitled to any protection at all under the statute, should remain protected only as to the innovation it introduced into the market, i.e. the once per week intramuscular injection. To hold otherwise would mean that the market for beta-interferon drugs for relapsing remitting MS will remain closed to competition for a total of ten years, in effect creating an "evergreening" of orphan protection.

The way to avoid this anomalous result is for FDA to allow the market to be open to competition against the original drug after its exclusivity expires. This would be consistent with the statute. If FDA chooses to award additional exclusivity for improved versions, it should be for the particular improvement introduced, not for the entire indication.

To require potential competitors to demonstrate superiority to both the original and a second product is a virtually impossible task. Further, if the first company, the originator itself, attempted to introduce a better version of its own drug, it would be precluded from doing so unless it demonstrated clinical superiority to the second drug in a head-to-head trial.

If FDA's current attitude prevails, the second "improved" drug would actually be receiving two rewards, (1) being allowed onto the market despite the pioneer drug's exclusivity and (2) receiving its own seven year period of exclusivity for the entire indication, not just the improvement. This reward is disproportionate to the innovation it introduced.

Finally, the designation of the second "improved" drug as an orphan in 1993 had nothing at all to do with its purported clinical superiority. At the time the sponsor of the drug simply entered a race to approval for relapsing remitting MS which was won by Betaseron. The improved features of Avonex were discovered much later, after the fact. There is no head to head evidence comparing Avonex with Betaseron.

Multiple sclerosis is a neurological disorder that affects women by a substantial majority. Relapsing/remitting disease eventually leads to progressive degeneration, where the patient no longer returns to normal functioning following a relapse. The Serono study results, published in the British medical journal *Lancet*, contain data showing that the higher dose of beta-interferon induced a far better response in patients with more advanced illness. The Serono high dose cannot be matched by simply increasing the frequency of injection with the currently marketed low dose products.

Serono has been pressing FDA for a response to its policy inquiry on the scope of exclusivity awarded to the second product, but to date none has been forthcoming.

FOX, BENNETT & TURNER

750 17<sup>TH</sup> STREET, N. W.

SUITE 1100

WASHINGTON, D. C. 20006

TELEPHONE: 202-778-2300  
TELECOPIER: 202-778-2330

ALAN R. BENNETT

March 18, 1999

By Hand

Elizabeth Dickinson, Esq.  
Office of the Chief Counsel  
Food and Drug Administration  
Parklawn Building, Room 6-57  
5600 Fishers Lane  
Rockville, MD 20857

Re: BLA #98-0261 -- Rebif® (interferon beta 1- $\alpha$ )

*Jr*  
Dear Ms. Dickinson:

This is a follow-up to the meeting between Serono Laboratories, Inc. and FDA regarding the orphan drug exclusivity granted to Betaseron and Avonex. As you know, it was suggested that I communicate directly with the Office of Chief Counsel to see whether FDA will change the initial interpretation that was offered, without waiving any right to a formal appeal by my client, Serono Laboratories, Inc.

**Background**

On July 23, 1993, Berlex received PLA approval and orphan drug exclusivity for its drug Betaseron to reduce the frequency of clinical exacerbations in ambulatory patients with relapsing-remitting multiple sclerosis. On May 17, 1996 -- prior to the expiration of the seven-year exclusivity period for Betaseron -- Biogen received approval for Avonex as an orphan drug, also for relapsing-remitting multiple sclerosis. FDA considers Avonex to be chemically the same as Betaseron for orphan drug exclusivity purposes but nevertheless approved Avonex during Betaseron's exclusivity period because FDA found that Avonex was a clinically superior product. In contrast to Betaseron, which is injected subcutaneously, Avonex is injected intramuscularly and was found to have fewer injection site reactions and a lower incidence of injection site necrosis than Betaseron, and this difference was found by FDA to make Avonex clinically superior.

Serono's product for multiple sclerosis, Rebif, is currently the subject of a BLA pending approval at FDA. Like Betaseron, Rebif is formulated for subcutaneous injection.

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Serono does not claim that use of Rebif would result in a reduced incidence of injection site necrosis similar to that of Avonex's.

In a letter dated February 24, 1999, the Office of Orphan Products Development (OPD) concluded that since Rebif is considered chemically the same as Betaseron and Avonex, Rebif cannot be approved during the exclusivity periods of either of those products unless Rebif is shown to be clinically superior to both products. OPD's rationale for this conclusion appears to be that any drug which contains the same active moiety as a drug with orphan exclusivity is considered to be the same drug, unless shown to be clinically superior.<sup>1</sup> Thus, since Rebif has the same active moiety as Betaseron and Avonex, and FDA does not currently view Rebif as a clinically superior product, Rebif is considered to be the same as both Betaseron and Avonex even though FDA considers Avonex not to be the same drug as Betaseron.

### Statutory Construction

As a matter of ordinary statutory construction, the OPD analysis is not a reasonable interpretation of the Orphan Drug Act. OPD's position is that Betaseron is the same drug as Avonex but that Avonex is not the same drug as Betaseron. In addition, OPD asserts that Rebif is the same drug as both Betaseron and Avonex even though Avonex is not the same drug as Betaseron.

This asymmetrical definition of sameness is irrational both as a matter of the English language and logical rules. It is simply not reasonable for OPD to assert that A is the same as B when B is not the same as A. Or that C is the same as both A and B even though B is not the same as A.

Moreover, OPD's interpretation, which is based on the FDA regulations, loses sight of the statutory provision that the regulations are implementing. Under section 527(a) of the Federal Food, Drug, and Cosmetic Act (FFDCA), if an orphan drug has exclusivity rights, FDA is prohibited from approving any other marketing application for "such drug" for the same rare disease or condition during the seven-year exclusivity period. There is no asymmetry in this statutory term. The statute allows only the determination that a second drug either is such drug previously approved or is not such drug. In other words, the statute establishes a test of whether the two drugs are the same or different. Nothing in the statute allows two drugs to be both the

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<sup>1</sup> The OPD letter and my letter both use the term "same active moiety" as a shorthand way to refer to drugs that are considered chemically the same under FDA's orphan drug regulations. Technically, that term applies only to small molecules. In the case of large-molecule drugs like interferon, the definition of chemical sameness in the regulations is more complex, but it is not relevant for the purposes of this discussion.

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same and different depending on which drug is the reference drug, as the OPD interpretation does.

To defend an asymmetrical definition of sameness as reasonable, FDA would have to demonstrate how that definition carries out the purposes of the Orphan Drug Act. As set forth in the rest of this letter, however, the definition serves no reasonable purpose to implement the Act and instead gives rise to numerous unreasonable and undesirable effects that are inconsistent with the purposes of the Act.

### **Effects of the OPD Interpretation**

OPD's interpretation of the Orphan Drug Act and FDA's implementing regulations would result in several serious adverse effects on the administration of that Act and on development of orphan drug products.

- **Extension of Exclusivity Beyond Seven Years**

The Orphan Drug Act was intended to provide seven years of exclusivity to an orphan drug, but only seven years. At the conclusion of that exclusivity period, Congress intended that other manufacturers would be able to enter the market with their versions of the drug. Under the OPD interpretation, however, the exclusivity of Betaseron would be extended well beyond the statutory seven-year period for reasons having nothing to do with Betaseron. Under the OPD interpretation, other manufacturers are prohibited from marketing their versions of Betaseron for ten years, until the expiration of Avonex's exclusivity period. This result is on its face inconsistent with the seven-year exclusivity period.

Although abbreviated applications for biologics are not available, OPD's interpretation would, of course, also govern drugs for which abbreviated new drug applications can be submitted under section 505(j) of the FDCA. In the case of an orphan drug approved by new drug application, the drug would be a reference listed drug for which manufacturers could obtain approval for copies by submission of ANDAs after the seven-year exclusivity period had expired. Under OPD's interpretation, however, the approval of a clinically superior second orphan drug product prior to the expiration of the first product's exclusivity makes the first reference listed drug unavailable for copying until the expiration of the second product's exclusivity. Any additional clinically superior product would extend the initial product's exclusivity even further beyond the intended seven years.

Not only does this result thwart the congressional intent to set a period of seven years exclusivity for orphan drugs, but it would also potentially deter FDA from approving a clinically superior orphan drug in the future. For example, suppose that five years into an orphan drug's exclusivity period a second manufacturer seeks FDA approval by NDA of a clinically

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superior version of a previously approved orphan drug. FDA would face a dilemma. If it approved the clinically superior version, generic competition for the first orphan drug would be delayed six or more years. If FDA denied or stalled approval of the clinically superior drug to avoid delaying generics, it would deny the public the benefits of the clinically superior product.

It is also noteworthy that, under the OPD interpretation, exclusivity periods that have expired can be reinstated. The FDA regulations permit orphan drug designation for a drug that is found, upon review of the supporting data, to be clinically superior to a previously approved drug. 21 C.F.R. § 316.20(a). Thus, even if the exclusivity period of the previously approved drug has expired, a clinically superior version of what would otherwise be the same drug can apparently obtain seven years of exclusivity. This exclusivity for the second drug would effectively reinstate the first drug's expired exclusivity, since any manufacturer seeking to copy the first drug could obtain FDA approval only by demonstrating clinical superiority to the second drug.

- **Evergreening**

OPD's interpretation would also allow the manufacturer of an orphan drug to extend its own exclusivity -- potentially indefinitely -- by making product improvements. Although Avonex was developed by a different company from the company that developed Betaseron, there is nothing in the OPD interpretation that would have precluded the manufacturer of Betaseron from developing a clinically superior version of its own product and obtaining an additional seven years of exclusivity for that product. Nothing in the FDA regulation defining "same drug" limits a clinically superior drug to one made by a company different from the sponsor of the comparative drug.

For example, the preamble to FDA's orphan drug regulations cited the example of a purer product as one that would potentially meet the standards for clinical superiority. 57 Fed. Reg. 62076, 62079 (Dec. 29, 1992). Under OPD's interpretation, it is easy to imagine that a naturally derived orphan drug product could be made purer in stages, with each successive improvement qualifying for seven years of exclusivity against all drugs having the same active moiety and intended for the same indication.

- **Threat to Development of Competitive Products**

OPD might be inclined to minimize the issues of extended exclusivity and evergreening on the theory that the development of clinically superior versions of orphan drugs is relatively rare. Regardless of how often clinically superior products are in fact developed, however, the threat that one might appear by surprise will endanger the development of competitive products for all orphan drugs. The OPD interpretation introduces a major

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unpredictability factor into development of competitive products and may significantly deter the investment necessary to support such development.

In the absence of the OPD interpretation, drug manufacturers can develop a generic or other competitive version of an orphan drug with the expectation that the product can be marketed at the conclusion of the innovator's seven-year exclusivity period. Under the OPD interpretation, however, a company planning a competitive product will have to decide whether to risk the investment to develop a product in light of the possibility that the exclusivity will be extended -- perhaps for many years -- by the unexpected appearance of a clinically superior version.

Moreover, the same risk exists even if the company is attempting to develop a clinically superior product. A company might risk substantial funds to develop a clinically superior version of a protected orphan drug, including head-to-head clinical trials, if it thought that its product could qualify under an exception to the innovator's exclusivity. Under the OPD interpretation, however, that planning and expenditure could be fruitless if a third party preempted the potential competitor by introducing a clinically superior version, including potentially a version that was clinically superior for an entirely different reason. If that happened, the head-to-head trials against the innovator would be worthless to support approval, since new trials against the second entrant would also then be required.

For example, suppose that, prior to approval of Avonex, Serono believed that Rebif was more efficacious than Betaseron and conducted head-to-head trials against Betaseron to establish that clinical superiority. Even if the trials had been successful, the approval of Avonex would have prevented approval of Rebif under OPD's interpretation. Even though Avonex broke Betaseron's exclusivity based solely on FDA's judgment of its improved safety, Rebif could be approved only if Serono conducted additional head-to-head trials demonstrating that Rebif was clinically superior to Avonex in terms of efficacy. This would be an irrational result in the particular circumstance, and the potential for its occurrence will seriously discourage companies from attempting to develop clinically superior versions of any orphan drugs.

- **Product Improvements Where There Are Two Approved Orphan Drugs**

OPD's interpretation appears to result in perverse and unjustifiable effects on product improvements if, as in the case of Betaseron and Avonex, there are two orphan drugs with the same active moiety that have been approved. Under its regulations, FDA is prohibited from approving any marketing application for the same drug during the exclusivity period. 21 C.F.R. § 316.31(a).

If "marketing application" in this regulation is interpreted to include supplemental applications, there could be no improvement made in Betaseron's product, manufacturing, or

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labeling during Avonex's exclusivity period unless Betaseron is shown to be clinically superior to Avonex. This would be the result because Betaseron is the same drug as Avonex and, therefore, no application for Betaseron could be approved.

Moreover, if Betaseron did develop an improvement that made the product clinically superior, it would apparently have to demonstrate its superiority against Avonex as a whole, not just with respect to the improved aspect. Thus, for example, if the manufacturer of Betaseron determined that it could reduce a side-effect by altering its manufacturing process or the recommended dosing regimen, it would be blocked from implementing that change unless it could show that the modified Betaseron would be clinically superior to Avonex. Under the regulations, direct comparative trials with Avonex might be necessary (and almost certainly would be necessary if the proposed improvement related to effectiveness). Moreover, FDA would somehow have to weigh the clinical value of the proposed improvement against Avonex's advantage in reduced injection site necrosis to assess whether the modified Betaseron had now become the clinically superior product. The situation that would ensue from OPD's interpretation would seriously obstruct, if not stop completely, improvements in the first orphan drug approved.

Note that, because of OPD's asymmetrical interpretation of sameness, the obstacles to product improvement affect only Betaseron, not Avonex. Since Avonex is not the same drug as Betaseron, the manufacturer of Avonex is apparently free to make any changes in its product, manufacturing, or labeling even while Betaseron is blocked from making similar changes. This would not be a reasonable interpretation of the Orphan Drug Act. It would certainly be a perverse outcome if the manufacturer of the first drug, which took the risk of developing an unknown drug, is competitively disadvantaged by being denied the opportunity to make product changes while the manufacturer of the second drug, which may have risked far less, enjoys the right to make such changes.

As indicated above, this situation would result if the term "marketing application" in 21 C.F.R. § 316.31(a) includes supplemental applications. Assume, however, that FDA were to exclude supplements from that definition and take the position that the manufacturer of Betaseron can make product improvements through supplemental applications notwithstanding Avonex's exclusivity. In that case, Betaseron could in theory perform the same studies on Betaseron that Serono conducted on Rebif and, if they were successful, obtain the same product and labeling changes for Betaseron that Serono is blocked from obtaining for Rebif. Since OPD takes the position that Betaseron is the same as Avonex and that Rebif is the same as Avonex, it is difficult to see how Betaseron and Rebif could be in such vastly different circumstances with respect to being blocked by Avonex's exclusivity rights.

Although the preceding discussion used Betaseron and Avonex as examples, the same barriers to product improvement would exist whenever FDA approved two orphan drugs

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with the same active moiety. OPD's interpretation would result in unreasonable obstacles to product improvement that cannot be reconciled with the purposes of the Orphan Drug Act.

### **Alternative Interpretation**

The problems outlined above all stem from OPD's implicit determination that an orphan drug that has the same active moiety as a previously approved orphan drug, and is approved under the clinically superior criterion, should have the same extent and degree of exclusivity against all other drugs as the first orphan drug. This policy is misguided. Instead of OPD's interpretation, the policy should be that an orphan drug approved as clinically superior obtains seven years of exclusivity with respect to those aspects of the drug that made it clinically superior. Such a policy would parallel Hatch-Waxman exclusivity, under which five years of exclusivity is available for a new chemical entity, and any subsequent three-year exclusivity periods apply only to the changes made in the product. Moreover, exclusivity limited to the improvement conforms better to the actual risk taken by the second drug's manufacturer - since the drug had already been shown to be safe and effective by the innovator, seven years' exclusivity over the entire product for a potentially modest improvement is not commensurate with the efforts deserving of reward.

This recommended result can be reached under the Orphan Drug Act by concluding that the first orphan drug is not the same drug as a subsequently approved, clinically superior orphan drug with the same active moiety. Under this approach, copies of the first approved drug could be approved when the exclusivity for the first drug expires, since they would be different from the clinically superior orphan drug. At the same time, no copy of the clinically superior drug could be approved until the expiration of its own seven-year exclusivity period. In Hatch-Waxman terms, both the first and second drugs would be reference listed drugs, and either would be available for copying upon the expiration of its exclusivity period. Thus, for example, in this case Avonex could have seven years of exclusivity for the administration of beta interferon by intramuscular injection, reflecting Biogen's innovation. Subcutaneously administered products could, however, be approved at the expiration of Betaseron's seven years exclusivity.

This alternative interpretation is not only consistent with the regulations, it is the only interpretation that is reasonable under the regulations and the Orphan Drug Act. Once the second drug is determined by FDA not to be the same as the innovator drug -- not to be "such drug" -- then the two drugs should be considered different drugs for all purposes. Accordingly, a third drug can be the same as, at most, only one of the two drugs.

This interpretation not only conforms to the common sense understanding of same and different, but it also eliminates all of the serious problems with the OPD interpretation outlined in this letter. Since Rebif does not claim the clinical superiority shown by Avonex,

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Rebif should be compared to Betaseron, and its approval should be effective upon the expiration of Betaseron's exclusivity.

### Conclusion

The question of whether OPD's interpretation is consistent with the statute must be assessed by determining whether it can be squared with the language of the statute and whether it results in outcomes that are consistent with the statute's purposes. As discussed above, the asymmetrical interpretation of sameness finds no support in the statute or in commonsense, and the effects of the interpretation frustrate the development of new and improved products. Along the continuum of product development - from improvements in the first product, to development of rival innovator products, to approval of generic versions - OPD's interpretation creates obstacles that cannot be properly viewed as intended by, or consistent with, the Orphan Drug Act. If the alternative interpretation suggested in this letter is adopted, however, FDA can avoid these unjustifiable outcomes while still rewarding clinically superior products with exclusive marketing rights to their improvements.

I would be happy to discuss any of these points with you in more detail. Serono would like to proceed with a formal appeal if this informal process appears to be unproductive, and accordingly, unless I hear from you sooner, I will call you about March 31 to determine where the informal process stands.

Sincerely yours,

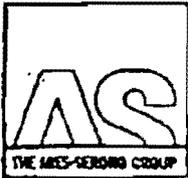


Alan R. Bennett

Attorney for Serono Laboratories, Inc.

cc: Michael A. Friedman, M.D.

Kathryn C. Zoon, Ph.D.



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**Serono**

PART OF THE ABBOTT-SERONO GROUP

SERONO LABORATORIES, INC.  
100 LONGWATER CIRCLE  
NORWELL, MA 02061 / USA  
(800) 421-4000  
TEL (781) 882-0000  
FAX (781) 871-6754

September 13, 1999

Jane Henney, M.D.  
Commissioner Food and Drug Administration  
HF-1  
5600 Fishers Lane  
Rockville, MD 20857

Dear Dr. Henney:

I am writing to follow up on correspondence directed to the agency last March on a policy question regarding Orphan Drug exclusivity. Specifically, I refer to a letter from our outside counsel addressed to the Office of Chief Counsel dated March 18, 1999. A copy is attached.

The letter was mentioned in a July meeting with Dr. Michael Friedman concerning our BLA for recombinant beta interferon in relapsing remitting multiple sclerosis. We understood from the meeting that the agency was preparing a response, but to date none has been received.

As indicated in the letter, the policy question deals with the extent of exclusivity that can or should be awarded to a subsequent product, which is otherwise the same as the first approved drug for an orphan indication, upon a finding that the product is "clinically superior."

We hold the view that if any exclusivity for the subsequent product is appropriate at all, it should be limited to whatever improvement or feature led to the finding of superiority. Otherwise, the result is an unwarranted extension of market exclusivity for the entire indication beyond the seven years specified in the statute.

We have been advised formally that the agency will require additional clinical data on our beta-interferon product to overcome the exclusivity awarded to previously approved orphan drugs that are chemically similar to ours, and we are proceeding accordingly. We still await an answer on the critical legal and policy question as to whether a product such as ours can enter the market after the initial seven years of orphan exclusivity protection as long as it does not duplicate those particular aspects of a subsequently approved product that have qualified for a finding of clinical superiority over the pioneer orphan drug.

I would greatly appreciate FDA's response to the March 18 letter on this issue at the earliest opportunity.

Sincerely,

Hisham Samra, M.D.



Dr. Kathryn Zoon  
April 5, 1989  
Page Two

Thus although drug prices are clearly not within the regulatory responsibility of FDA, it is very important that the agency understands how important it is to approve generic drugs just as soon as a patent – or exclusivity – expires on a drug or biologic. Competition lowers prices and makes important treatments accessible to more patients.

In this regard, the attached letter raises the question of why Betaseron's exclusivity will be extended beyond seven years because FDA will not approve Rebif until Avonex' exclusivity expires in 2003. I do not have an answer to this question. It is true that the Orphan Drug Act was not meant to shield drugs or biologics beyond seven years. Since FDA has decided that Rebif is the same as Avonex and Betaseron, it stands to reason that Betaseron should have competition in the year 2000. Moreover, since Rebif's side effect profile is similar to Betaseron, it is reasonable to assume that it is the same drug as Betaseron.

I look forward to hearing from you.

Very truly yours,



Abbey S. Meyers  
President

ASM:aa

Enclosure

cc: Dr. Michael Friedman, Associate Commissioner FDA

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HEADLINE: Experts Ask Why So Few Take Drugs for M.S.

BYLINE: By

BODY:

Four months ago, Valerie Millerick finally made a decision that she had been putting off for years: She began taking weekly injections of a drug called Avonex, to treat multiple sclerosis.

Ms. Millerick, who is 54, had been living with the illness for about two decades, and for most of that time she did not think she was sick enough to need regular treatment.

But multiple sclerosis can be insidious. It often takes a course of remissions and relapses, and recent studies have shown that even during remissions, the disease may be silently eating away at the nervous system. It destroys myelin, the protective sheath around nerve fibers in the brain and spinal cord, and gradually begins to damage the nerves themselves. Although it is not commonly fatal, it can cause permanent weakness, paralysis, loss of eyesight and memory and slowing of thought processes.

Suddenly last year, Ms. Millerick felt herself losing ground to repeated attacks of intense fatigue and weakness. But she works full time as head of a nursing agency that she founded in Valley Cottage, N.Y., and she would not give in to the disease.

"It was battering me," she said. "Every time you have an attack, it leaves you with a little bit of residual damage." Her right hand and leg were weakened permanently, and to walk any distance she needed a cane.

"I saw myself in a wheelchair, and that's not where I want to be," she said. "I had to do something to stop it."

There is no cure for multiple sclerosis, but Avonex and two other drugs, Betaseron and Copaxone, can keep it from getting worse. For most patients, each drug produces a 30 percent reduction in the frequency of flareups and the progression of the disease.

Since she began taking Avonex, Ms. Millerick has not had another attack. "I think I made a wise choice," she said, "but I wish I had made it a few years ago."

Even though scientists have hailed the drugs as a breakthrough, patients have been slow to take them. Last fall, the Multiple Sclerosis Society reported that only 18 percent of the people who could benefit from the drugs were using them.

That is something that the National Multiple Sclerosis Society is trying to change. It may be human nature to deny the severity of an illness and to put off taking medicine and leave well enough alone. But experts have come to believe that multiple sclerosis patients who do so may suffer irreversible losses that medication might have prevented or at least delayed.

Betaseron has been available in this country since 1993, and Avonex since 1996. Both are forms of beta interferon, an artificial version of a natural substance made by the immune system. Copaxone, which also acts on the immune system, was approved in this country in 1997. The three drugs are the first ones ever proven to slow the underlying course of multiple sclerosis, which is thought to be the result of a malfunctioning immune system that turns against the patient's own tissues.

In November, the society formally recommended that every patient with the relapsing form of the disease -- the most common type, affecting 70 percent of the 300,000 to 350,000 patients in the nation -- should start taking one of the three drugs as soon as the condition is diagnosed.

But doctors also acknowledge that the treatments can be difficult. The drugs cost \$1,000 a month and must be given by injection -- daily, every other day or once a week, depending on the drug. The course of treatment is indefinite, probably lifelong. The interferons can cause flu-like fever, chills and aches, and pain and swelling at the injection site. For all that trouble, the drugs do not cure the disease and may not make people feel better.

"People have to take these treatments on faith," said Dr. Stanley van den Noort, chief medical officer of the National Multiple Sclerosis Society and a professor of neurology at the University of California at Irvine. "For a year or two, the drugs don't make them feel better. But I've had patients on Betaseron for 5 or 6 years, and you couldn't get them off with pliers. They love it."

Dr. van den Noort said doctors, patients and insurance companies all contributed to the low use of the drugs. "A lot of doctors are reluctant to use these drugs because of side effects," he said. "They tell patients, 'You're too mild, you don't need this.'"

That is what many patients want to hear. And, he added, insurers and health maintenance organizations do not promote treatment, either, because they would rather not pay for it. Part of the reason the society issued its recommendations was to make it clear to insurers that patients need the drugs, Dr. van den Noort said.

Both doctors and patients have to get used to the idea of using a medicine that, at best, will maintain the status quo, rather than improve it. Mimi Mosher, a 37-year-old graphic designer in Mechanicsville, Va., who has taken both Betaseron and Avonex, said that limited goal can be hard to accept.

"Initially, I had a misconception," Ms. Mosher said. "I thought I had pretty well educated myself and yet I still felt, 'I'm not getting any better from this. Why am I taking it?' I was expecting some radical event. What's carved in your mind is that medicine is supposed to make you better, even though I was fully aware that's not how interferon works. It's a slow-you-down, maintenance kind of drug."

Ms. Mosher said that after taking Betaseron for two years, she became skeptical about it and stopped for about 8 months. "I had more fatigue, and my endurance dropped," she said. "I was too tired even to speak, or to listen to my son."

But when she went back on medication (she switched to Avonex), she regained her energy. "I feel that I have basically leveled off with the disease," she said.

Other patients remain wary and skeptical of new drugs, sometimes because of bad experiences. One, a lawyer who did not want her name printed, said drugs she was given years ago for eye problems from multiple sclerosis were later found to cause the very problem they were supposed to treat.

"It's science like this that makes me cynical," she said. "They know something now, but what will they think in 20 years?"

She prefers to treat herself with acupuncture, vitamins and other supplements and a vegetarian diet that meets the low-fat regimen that is recommended for all patients with multiple sclerosis. But she will also enter a study of Estriol, a hormone produced by pregnant women. It is experimental, but she was encouraged by what she read about results in animal tests, and the natural aspect of it appealed to her.

"It's a gut feeling, I guess," she said.

Lynn Wilmott, who has multiple sclerosis and runs support groups for the Southern California chapter of the national society, also had bad experiences with treatments, including severe side effects from both Betaseron and Copaxone. But about a year ago she decided to try Avonex anyway.

"I'm loving it," she said. "My memory is much better. I can handle more than one project at a time without major confusion. "

Before taking the drug, Ms. Wilmott had lost some of her eyesight and her ability to walk, and she does not expect to regain them. But she hopes to hold her ground.

"You have to be proactive," she said. "You can try one drug, and if it doesn't work, try another. This disease causes definite, permanent nerve damage and brain atrophy. Stop it while you can."

<http://www.nvtimes.com>

GRAPHIC: Photos: Valerie Millerick did not think she was sick enough to take a drug for her M.S. Now she wishes she had taken it earlier. (Joyce Dopkeen/The New York Times); Mimi Mosher said her doubts about taking an M.S. drug were based on a misconception about what it was supposed to do. (Scott Robinson for The New York Times)

TO: CHRIS / DEVAR AW

FROM: JAW

THE WHITE HOUSE

Office of the Press Secretary  
(New York, New York)

Internal Transcript

October 7, 1999

INTERVIEW OF THE PRESIDENT  
BY  
JOHN ROBERTS OF CBS~~Sheraton New York Hotel and Tower~~  
New York, New York

3:40 P.M. EDT

Q Mr. President, sir. Good to meet you; how are you?

THE PRESIDENT: Good to see you.

Q So, you know the issue, sir. You've been trying to address it, the idea that there are 15 million senior citizens in this country who don't have Medicaid coverage for prescription drugs, Medicare coverage. What does it say about a country, sir, where many people have to go outside of the country to buy drugs that they can afford?

THE PRESIDENT: Well, it's wrong. And it happens because we have about three-quarters of our senior citizens need prescription drugs that they simply can't afford. They don't have access to any coverage, or the coverage they have is too expensive and too limited. And in Canada and in many places, drugs made in America are cheaper than they are here because bigger units can buy discounts.

Now, this proposal I made to reform Medicare is totally voluntary -- no senior has to buy a prescription drug coverage if he or she doesn't want it. But if they do buy it, then a private group -- not the government -- would be able to get the drugs at a lower cost because they would be buying them in bulk. And I think it's fair. It will not adversely affect the drug companies. It will increase their volume, even though the drugs, individually, will be cheaper. They will still come out way ahead. And our people will be treated more fairly and they won't have to depend upon whether they're on the Canadian border to run across the line to buy drugs they can afford.

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Q What do you think about the idea of allowing pharmacies to re-import drugs, parallel importing for senior citizens and allow them access to the cheaper prices that they would pay in Canada?

THE PRESIDENT: You're the first person that ever asked me that. I don't know. But I'll look into it. It's an interesting idea. I never thought about it.

Q That's Congressman Sanders' idea. He has proposed to allow pharmacies to re-import drugs from Canada or Mexico. There has been some question as to whether or not that would be legal because of FDA regulations. But that's the idea that he is proposing.

THE PRESIDENT: Well, if you could preserve their safety and quality, that there were some assurance of that, I would think it could be done. And it might work well along the Canadian border for Vermont, where Congressman Sanders lives, and for the other states along the border.

Then the further you get away from the border, the question is will the transportation cost back more than offset the money that you would otherwise save. I don't know the answer. You're the first person that's ever asked me that. But I'll look into it.

Q Now, the drug companies have been saying that even under your plan, which would allow Medicare to buy drugs in bulk, it would decrease the revenue stream to the point where research and development would be stifled. I mean, would you look at the profits they've been making in the last few years -- is that a legitimate argument?

THE PRESIDENT: No. No, you know, they said that over and over and over again. American drug companies charge American citizens far more money for the same pharmaceuticals than they charge Europeans, Canadians, Mexicans, anyone else.

Q Does that seem right?

THE PRESIDENT: No. They say they do it because we bear the full cost of -- the research and development cost -- and they can't put it off on any of the others because the government controls the prices. That's what they say.

So I think if that's true, then the United States and its people have been awfully good to our drug companies. They've been willing to pay higher prices for drugs made in America than

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people in other countries do, and I think they owe it to the seniors to get off this high horse and stop trying to beat this attempt to extend medical coverage to seniors for prescription drugs.

People that live on fixed incomes ought to be able to get the benefit of discounts you get when you buy in bulk. This is not government regulation, this is market power. A lot of these drugs they have long since recovered the research and developments cost, long since. And I just think it's wrong for our people either not to be able to get them at all or to pay so much more than others do. And this is one way to sort of split the difference between their position that they need higher profits to invest in research and development, and the very low cost that they can get if they happen to live close enough to the Canadian border to cross it.

So I would like to see Medicare cover prescription drugs on a voluntary basis so our seniors can get discount prices. It's very important.

Q The ideas that have been floated in the Senate, which ostensibly are voucher systems, would you agree with that type of system to pay for prescription drugs?

THE PRESIDENT: Well, it wouldn't be as effective as the proposal we've made because it would be more difficult to get the benefit of discounts. And, therefore, over a few years it would be harder to keep the premiums down.

But, as I said, I would like to see the members of Congress in both parties engage with us on this, let's work it through, let's come up with something -- you've got three-quarters of our seniors in trouble out there and we ought to do something about it.

Q In terms of national priorities, how important is this?

THE PRESIDENT: Oh, I think it's very important. The big challenges facing our country right now, at the top of those challenges are what to do about the aging of America as more of us live longer -- that means we have to save Social Security and reform and modernize Medicare; and the children of America -- we have to give all of our kids a world-class education with the most diverse student population ever.

Those are the big challenges we face. And to me this is a big part of it. You're going to have -- the average 65 year old person today has a life expectancy of 82. The people being born today, if the human genome project works out right, might have a

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life expectancy of 100. But if that's true, in order to maintain their quality of life and their health and not bankrupt the hospitals, we'll have to keep more and more of them well with the proper kind of drug treatment programs.

So you want the drug companies to be able to continue to pioneer new drugs, but they've got to be affordable and they have to be accessible.

Q Thank you for your time, sir, I appreciate it.

THE PRESIDENT: Thank you.

END

3:46 P.M. EDT

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DEPARTMENT OF VETERANS AFFAIRS  
Veterans Health Administration  
Washington DC 20420

Allen R + Drug File

OCT 20 1999

In Reply Refer To:

The Honorable Thomas Allen  
U.S. House of Representatives  
Washington, DC 20515

Dear Mr. Allen:

This letter is intended to provide clarification regarding the Administration's views on H.R. 664, which would extend discounts for pharmaceuticals to the Medicare population by requiring pharmaceutical manufacturers to provide discounts to retail pharmacies. As you know, the Federal government pays for pharmaceuticals that are purchased by a number of different agencies, including the Department of Health and Human Services (HHS), the Department of Defense (DOD), and the Department of Veterans Affairs (VA).

There are many ways to analyze the direct and indirect impacts of proposals such as those in H.R. 664, and the overall costs of such a proposal, if any, are unknown at this time. Our prior correspondence on this issue argued that H.R. 664 could have a negative impact on VA's ability to negotiate the lowest possible prices for drugs listed on the FSS, and other prices negotiated by VA, because drug manufacturers would be unwilling to continue to grant us discounts at prior levels. Others have argued that making drugs available to pharmacies at the lowest possible price would not undercut VA's ability to negotiate for the lowest price with drug manufacturers. The GAO has also concluded that the effect on schedule prices of opening up the FSS will "ultimately depend on the outcome of negotiations between VA and drug manufacturers. Because of the uncertainties related to these negotiations, it is not possible to predict how schedule drug prices would change. . ." (GAO/HEHS-97-60, June 1997). ||

We look forward to working with you and others in Congress on this issue.

Sincerely,

Thomas L. Garthwaite, M.D.  
Acting Under Secretary for Health