

## Achieving Targeted Pharmacy Trend With Clinically Informed Trend Analysis

“You should just say no to drugs.  
That will drive the prices down.”

Geechy Guy

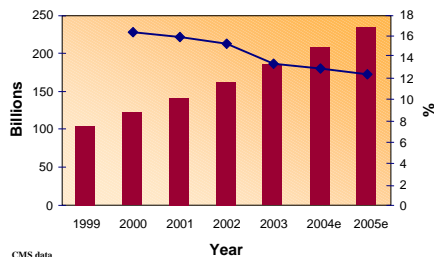
### Clinically-Informed Pharmacy Trend Analysis

#### Agenda

- Pharmacy trends
- The pharmaceutical industry
- Clinically-informed trend analysis high level overview
- Micro and macro trends
- Clinically-Informed trend analysis illustrations
- Wrap up

## Pharmacy Trends

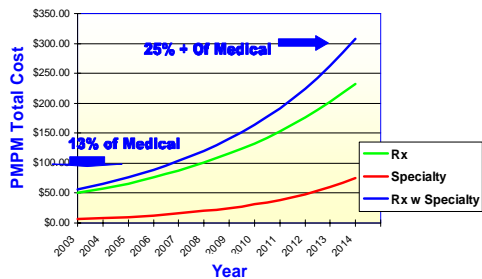
### Prescription Drug Cost and Annual Percent Increase



### Even in Down Cycle Pharmacy Trends Continue to Outstrip Medical

- Medco
  - 2004 – 2006: 9 – 13%
- Express Scripts
  - 2004: 10.6% without specialty
- Caremark
  - 2004: 9.9%
- Prime Therapeutics
  - 2004: 5.7%, or 8.3% adjusted for demographics
  - 2005-2006: 8% - 12%
- IMS
  - 2005 – 2009: 7 – 10%

## Where Rx is Trending



## Current Rx Cost Cycle Looks Like 1993-94

- 1993 – 1994
  - Cost focus in macro sense
  - Patent expiration issues
  - Regulatory scrutiny
  - Lack of new products
  - Pharmacy trends of 7% - 8%
  - Then double-digit trends for 9 years
- 2004 – 2005
  - Similar list
  - \$9.7b of drugs went generic in 2004 & \$7.8b in 2005
  - There is currently a wave of top-selling brands going generic
  - Value of recent launches is less than patent expirations
  - Safety:
    - Suicide & antidepressants in adolescents
    - Recalls of Vioxx & impact on COX-2s

## Current Rx Cost Cycle - Continued

- 2006: Drugs accounting for \$12.6b will go generic
  - Zocor, Zoloft, Zithromax, Pravachol, Allegra & others
- IMS reports sales growth is down
  - Up 5.5% in June '05 over June '04 vs 8.3% in '05
  - Yet number of Rx's is up @ 6% YTD vs 3% in '05
- Drugs going straight to OTC from brand, like Prilosec
- Reasons given by Lehman Brothers
  - Generic prescribing is up
  - Benefit design changes
  - Retail outlets holding less inventory (35 days vs 60 days)
  - Specific products such as Vioxx, Bextra

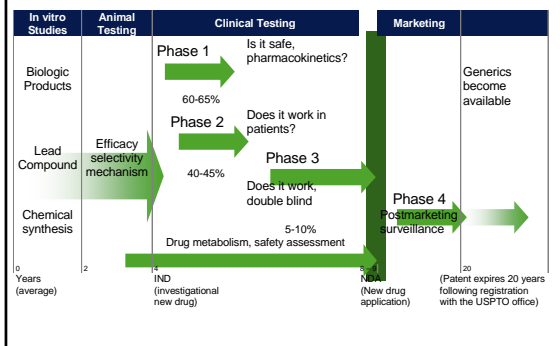
## Current Rx Cost Cycle - Continued

- Pharmacy same store growth @ 4%
  - Lowest in years
- Top drug companies report slow sales
  - Down 2.4% through June '05
- Mail Order utilization is up 20% in '05
- Brand prices are up around 6%
  - Similar to last year
- U.S. Pharmaceutical Industry Sales up 8%
  - First time in single digits since 1995
  - They will do everything possible to "improve" on this

## The Pharmaceutical Industry

- Knowledge of how the industry works is an important foundation for doing pharmacy trend analysis
  - Pricing of drugs
  - Reactions to successes & failures
  - Reactions to patent expirations
- Knowledge of where the dollars are being invested is a leading indicator
  - Dollars to influence consumers
  - Dollars to influence physicians
- Knowledge of drug approval process helps

## Drug Development



## Pharmaceutical Companies

- Invest 18% of sales revenue in R&D & testing
  - \$36b + \$10b for biotech
- Impact of this level of investment in search of an ROI
- Near monopolistic pricing
- Price inflation influenced by
  - Utilization
  - Market basket for that company
  - Market time remaining

## Be Aware of Prescription Drug Pricing

- Pricing Strategies
  - Drugs with:
    - Important therapeutic gains = 3x competitor's cost
    - Modest gains = 2x higher
    - No difference = equivalent price
- What determines annual price increases?
  - Estrogens tell the story
    - Lower than expected utilization results in higher unit cost
  - Fewer new drug introductions = higher unit costs

## Track the Blockbusters

- Blockbusters – Historically have been defined as products exceeding 1 billion in retail sales
  - In 2004 34 oral products achieved this number
    - 4 have become generic and 1 is generic (*Allegra*)
      - Neurontin, Oxycontin, Duragesic, hydrocodone / APAP
    - 2 have been removed from market
      - Vioxx & Bextra
    - 13 of 33 Brand products have had or are "new formulations" of previous blockbuster drugs that have been approved in past 24 months
    - 21 of 33 totaling \$42 Billion have lower cost "clinical appropriate" alternatives available
- Blockbusters are becoming harder to come by

## Pharmaceutical Company Generic Strategies

- Create an "authorized agent" to compete with exclusive generic
- Create a combination product
  - Combine a threatened product with a patent-protected one
- Line extension
  - Move patients to next generation product before generic comes out.
- Patent litigation (Multiple patents slow generic introduction)
  - Omeprazole – Drug coating is in litigation
  - Neurontin - Similar

## Evergreening

- Caduet : atorvastatin & amlodipine
  - \$8,400,000,000
- Wellbutrin XL: once-daily bupropion
  - \$2,000,000,000
- Symbyax: olanzepine & fluoxetine
  - \$2,800,000,000 + fluoxetine
- Vytorin: simvastatin & ezetimibe
  - \$6,000,000,000
- Tricor reformulation: Fenofibrate
  - \$600,000,000

**Pharmaceutical Industry  
Marketing Sophistication: Detailing**

- There are 100,000 pharmacy reps
  - 70,000 more than 10 years ago (Verispan)
  - \$15.5b spent on free samples (IMS)
- Physician detailing is more sophisticated
  - LTV (Lifetime Value) of physician is measured
    - Net present value of an MD's future prescribing
    - Less time is spent on low LTV's (older, etc.)
  - Physicians are segmented
    - Attitudes, behaviors and demographics are assessed
    - Message to a physician is targeted to them

**Clinically-Informed Trend Analysis  
High Level Overview**

**Starting Point for Clinically-Informed Trend Analysis**

- Behaviors of pharmaceutical industry are predictable
- Introduction of new drugs is knowable
- Generic Introductions are scheduled in advance
- ROI needs of Pharma will continue
- Paying attention to the details will result in a more accurate forecast

**What is Clinically Informed Trend Analysis?**

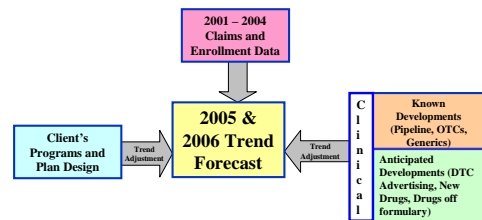
A clinical pharmacist adds knowledge of literature, pipelines, news, diseases as they relate to specific drugs.

The analyst translates the clinical input into factors that override standard regression analysis for those specific drugs.

**Clinically-Informed Trend Analysis =  
More Predictable Outcomes**

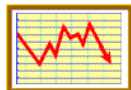
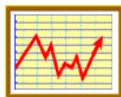
- Regression analysis does not *anticipate*
- Foresight = 24 month advantage over hindsight
  - In spring of '05 you need to price for '06
  - If you wait to see claims experience you will adjust for '06 experience in the spring of '07
- Provide ability to control trend rather than react to trend
  - Adjust plan designs
  - Implement clinical programs

**Pharmacy Trend Forecasting Process**



## Regression vs Clinically Informed Analysis

Using clinically informed trend analysis you include knowable, scheduled events that can alter the future trajectory of the trends of the past 24 months.



With this approach you are aware of the potential cost impact of many upcoming events that will impact cost, and you can respond to them before they occur.

## Regression vs Clinically Informed Analysis

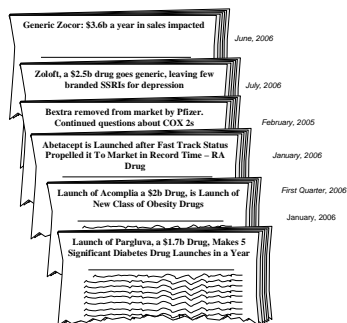
Regression	Clinically Informed
<ul style="list-style-type: none"> <li>■ Uses macro data making it fast</li> <li>■ 2003 – 2004 data will determine 2006 pricing</li> <li>■ Method works for medical</li> <li>■ Dollars involved in pharmacy are not that great</li> </ul>	<ul style="list-style-type: none"> <li>■ Uses drug specific data</li> <li>■ 2005 and 2006 “knowable” information will trump trendline data</li> <li>■ Pharmacy industry is different from medical with drug pipeline information and generics scheduled events</li> <li>■ Pharmacy dollars are a greater percent of total healthcare every year</li> </ul>

## Micro and Macro Trends

### Micro Trends

- Events relating to a drug class or a single drug
- New drug launches
- Drugs Going Generic
- Drugs with safety concerns
  - Potential to be withdrawn from market
- FDA approvals for new indications
- Any drug-specific information pertaining to “significant” drugs

### Some currently known micro events



### Micro Trends Safety Concerns for 2004

- Bextra (valdecoxib)
  - Withdrawn from market in April 2005
- Meridia (sibutramine)
  - Indication: Weight loss drug
  - Concern: Increased blood pressure
  - Prime's Position: Limited efficacy as diet aid and may raise blood pressure possibly attenuating any weight loss associated with the product
- Accutane (isotretinoin)
  - Indication: Severe Acne
  - Concern: Birth defects
  - Prime's Position: Very effective agent for severe Acne with well known teratogenic effects resulting in risk management program
- List, compiled by David Graham, also includes Crestor & Serevent

### Micro Trends 2005 approvals – New Formulations

Name	Company	Date	Use
Zmax (zithromax)	Pfizer	Jul 2005	Single-dose version of azithromycin
Asmanex (mometasone)	Schering-Plough	Mar 2005	Inhaled corticosteroid; launch Fall 2005
Boniva (ibandronate)	Roche	Mar 2005	Once-monthly bisphosphonate
BIDil (isosorbide dinitrate/hydralazine)	NitroMed	Jun 2005	CHF in African Americans
Tramadol ODT	Biovail	May 2005	Oral disintegrating dosage form
Triglide (fenofibrate)	SkyePharma	May 2005	
Aczone (dapsone)	Atrix/Fujisawa	Jul 2005	Topical acne

### Micro Trends Potential Patent Expirations

2005	Paxil CR, Amaryl, Mobic, Pandel cream, Geref, Livostin, Biaxin, Zithromax
2006	Pravachol, Zocor, Zofran, Zoloft, Wellbutrin XL, Emadine, Apligraf, Proscar, Retrovir, Provigil, Doxil, Maxaquin
2007	Aceon, Mavik, Actiq, Clarinex, Geodon, Imitrex, Tequin, Zyrtec, Norvasc, Lotrel, Coreg, Meridia, Aloclil
2008	Kytril, Effexor/XR, Serevent, Advair, Depakote, Dovonex, Zymar, Fosamax, Zerit, Risperdal, Camptosar, Casodex, Trusopt
2009	Prevacid, Avandia, Glyset, Xenical, Acular, Lamictal, Topamax, Valtrex, Vexol, Avelox
2010	Cozaar, Hyzaar, Precose, Skelid, Arimidex, Hycamtin, Trizivir, Combivir, Epivir, Abilify, Gemzar, Zagam
2011	Lipitor
2012	Plavix

### Micro Trends Future Generic Entries

Brand Drug	2004 Sales	% Change	Strategy
Zocor	\$ 3,150,892,000	2.8 %	Vytorin
Pravachol	\$ 1,522,955,000	- 3.7 %	Pravigard
Neurontin	\$ 2,000,077,000	3.1 %	Lyrica
Paxil	\$ 1,500,000,000*	- 35.4 %	Paxil CR
Celexa	\$ 856,665,000	- 29.5 %	Lexapro
Allegra	\$ 1,260,443,000	- 6.6 %	Allegra OTC
Ambien	\$ 1,719,253,000	18.3 %	Ambien CR
Norvasc	\$ 1,883,014,000	9.8 %	Caduet
Zoloft	\$ 2,622,801,000	6.6 %	New Indications

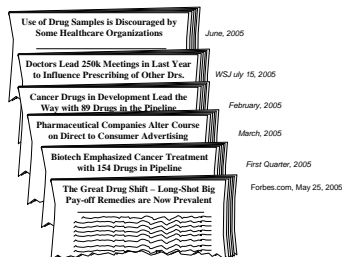
\* 2003 sales  
Source: Drug Topics March 2005

### 2004 Top 10 US Brand Drugs by Sales

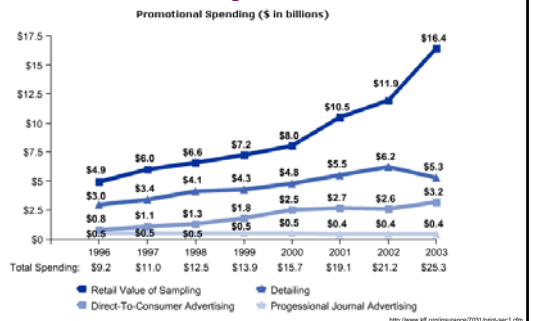
Drug Name	Sales (Billions)	Change from 2003
Lipitor	5.9	10.9 %
Prevacid	3.2	- 4.8 %
Zocor	3.2	2.8 %
Nexium	3.0	19.0 %
Zoloft	2.6	6.6 %
Advair	2.3	22.7 %
Effexor XR	2.3	19.4 %
Plavix	2.2	30.4 %
Celebrex	2.1	6.0 %
Neurontin	2.0	3.1 %

Source: Drug Topics March 2005

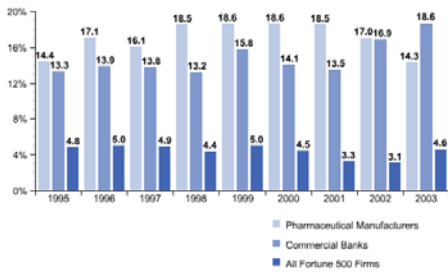
### Some currently known macro events



### Macro Trend Trends in Promotional Spending for Prescription Drugs, 1996-2003



### Macro Trends Profitability Among Pharmaceutical Manufacturers Compared to Other Industries, 1995-2003



http://www.fif.org/resources/7031.pdf&doc1.doc

### Macro Trends Active Areas of Development

Current Clinical Trials (Phase III, pre-registered, registered)	
Cancer	89
CV Disease / Hyperlipidemia	38
Arthritis / Pain	30
Bacterial Infections / Mycosis	30
Viral Infections / HIV	30
Allergy / Asthma / COPD	18
Anxiety / Depression / Schizophrenia	17
IBS / Crohn's Disease	17
Alzheimer Disease / Cognitive	14
Diabetes	14
Thrombosis / Stroke	14
Hormone Deficiency / Osteoporosis	13

IMS Health; MIDAS, MAT Dec 2003

### Macro Trends

- Pharmaceutical industry lobbying dollars reach record levels
- The U.S. = 46% of global market of \$550 billion
- Global market grew 9% in 2003 & 7% in 2004
- Mail Order grew 17.9% in 2004
- Reputation of pharmaceutical companies drops
  - 44% say it does a good job for consumers
  - Down from 79% just 7 years ago

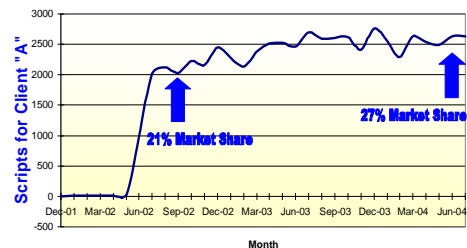
### Macro Trends Marketing Sophistication on the Rise

- Length of time to peak sales is a key success factor (Partnerships have increased to help co-promote)
- Speed in opening multiple markets increases revenue (Levitra and Cialis rolled out to 5 markets in 3 months)
- Launching in the U.S. first when possible (Creates a sustainable competitive advantage)
- Priming the market in advance of FDA approval (Raising awareness helps with launch of product)

### Macro Trends Marketing Sophistication: Advertising

- Consumer advertising up 22% in 2003 over 2002
  - 1/3 is print media
  - Current trend is to cable TV and Internet – Away from Network TV
  - Return on Investment is good
- Targets
  - Larger markets
  - Chronic conditions
  - Higher priced products
  - Products with no clear medical advantages over competition

### Uptake of Nexium

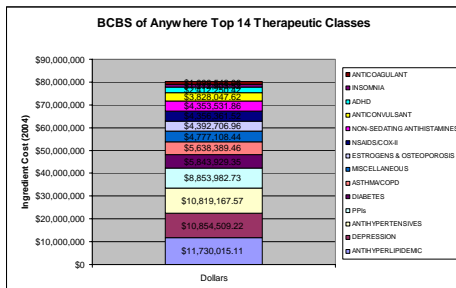


# Clinically-Informed Trend Analysis Illustrations

## Clinically-Informed Trend Analysis

- Focus on top 14 therapeutic classes
  - Based on opportunity
- Track upcoming events
  - Drugs
  - T-classes
- Create a table to override regression analysis
  - Input factors for known events
  - Input factors where known clinical programs are planned
- Know value of clinical programs

## 2004 Relative Rank of Top Therapeutic Classes



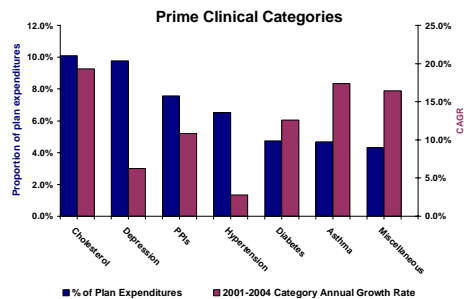
## Clinically-Informed Trend Analysis Top 14 Therapeutic Categories Review

- ADHD** –In recent years, more adults are being diagnosed and treated for ADHD.
- Anticoagulant** – Plavix use has rapidly grown over the past 5 years. It's now approaching one of the top five drugs overall.
- Anticonvulsant** – The greatest management opportunity is to control the 60 to 80% of use considered "off-label", for which little supportive data are available.
- Antihyperlipidemic** – This class is trending at 15 to 20% each year. 2006 will bring generic entries for Zocor and Pravachol.
- Antihypertension** – This class represents the greatest generic utilization opportunity. **Asthma/COPD** –As generic inhalers are phased out by 2007 due to environmental concerns, we will need to manage potential cost increases due to the shift to more expensive medications.
- Depression** –As SSRIs become generic, we anticipate a continued shift in marketing strategies by pharmaceutical manufacturers to a new class, called SNRIs.

## Clinically-Informed Trend Analysis Top 14 Therapeutic Categories Review (cont)

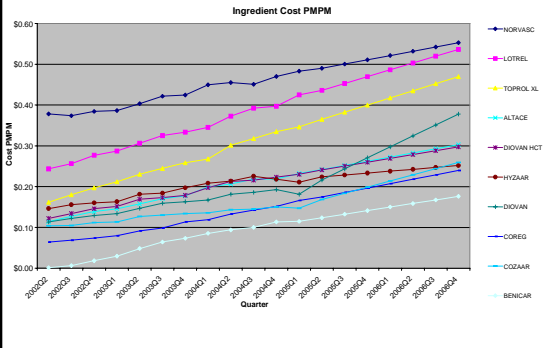
- Diabetes** – Look for tremendous growth in the diabetes category.
- Estrogens/Osteoporosis** –Utilization in this class is at it's lowest and will only increase with new products.
- Insomnia** – represents the potential for tremendous growth. By one estimate, one-third of the U.S. population suffers from insomnia.
- Nonsedating Antihistamines** –OTC medications such as Claritin have given payers the option to remove this class from coverage.
- NSAID/COX-2** – With both Vioxx and Bextra withdrawn from the market, safety in this category remains a major concern.
- PPI's** –As the cost of generic omeprazole decreases, payers should take advantage of programs designed to encourage generic use.
- Miscellaneous/Combination Drugs** –The pharmaceutical industry is increasingly combining two different drugs into one pill as a way to market new products

## Compounded Annual Growth Rate by Category





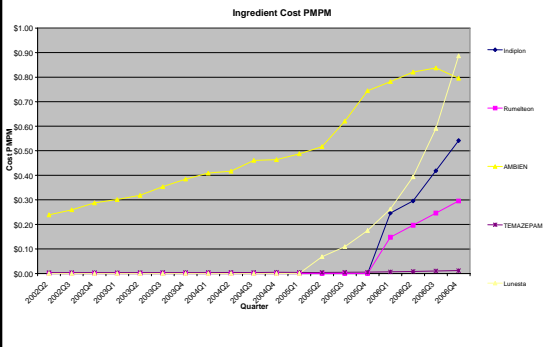
### Pharmacy Trend Forecast by Therapeutic Class – Antihypertensives



### Tracking Events Involving Hypertension

Name	Company	Notes	Dateline
nebivolol	Mylan	Beta-blocker. Marketing message: affects NO, which other beta-blockers may not	Approvable May 2005
lercanidipine	Forest	Dihydropyridine CCB	Approvable Aug 2002; approval no earlier than '05 (perhaps '08)
aliskiren	Novartis	Renin inhibitor	NDA filing 1 <sup>st</sup> H '06
Amvaz (amlodipine maleate)	Dr. Reddy's	Different salt formulation from Norvasc (amlodipine besylate)	2007
Vanlev (omapatrilat)	BMS	Vasopeptidase inhibitor	Approvable Oct 2002

### Pharmacy Trend Forecast by Therapeutic Class – Insomnia



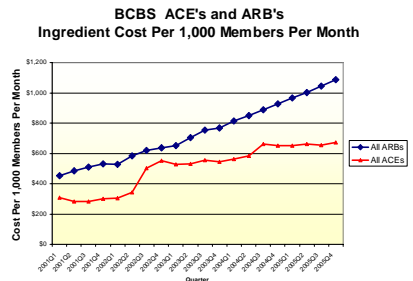
### Tracking Events Involving Insomnia

Name	Company	Notes	Dateline
Somposure (IR + CR indiplon)	Pfizer/ Neurocrine	Non-benzo GABA-A agonist	User fee: Feb 2006
Ambien CR (zolpidem)	Sanofi-aventis	CR approval with IR generic entry	Approvable Apr 2005; expects launch '05
zolpidem ODT	Biovail	rapidly-dissolving, orally-disintegrating formulation	Oct 2006 (Ambien patent exp.)
Silenor (doxepin)	Somaxon	Low dose formulation of antidepressant	Approval expected late 06
Gaboxadol	Merck	non-benzodiazepine direct-acting GABA-A receptor agonist for insomnia	NDA filing '07

### Implement Rx Management Tools to Help Manage Specific Categories

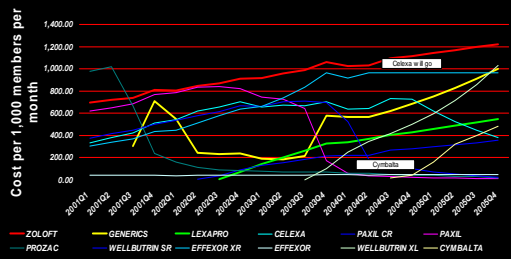
- Mandatory Generics
- Step Therapy
- Reference Pricing
- DUR programs
- Fertility Drug policies
- Diabetic Supplies – Keep cheap
- Obesity – Off-label use control
- Injectables – Specialty contract
- Prior authorization
- Generic formulary
- Be sure you are considered highly managed

### Managing Your Trend ACE/ARBs



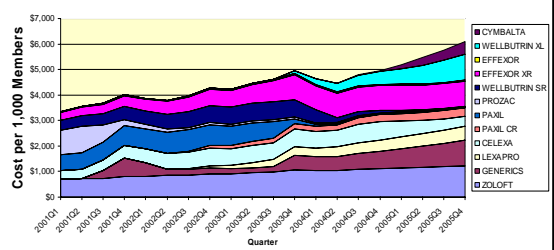
### Clinically-Informed Trend Analysis

#### Antidepressants



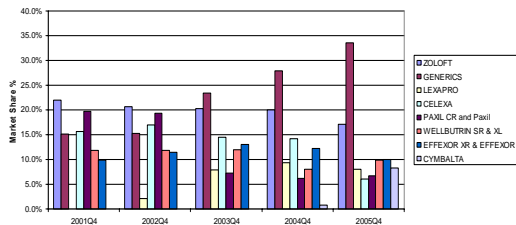
### Clinically-Informed Trend Analysis

#### Anti-depressants



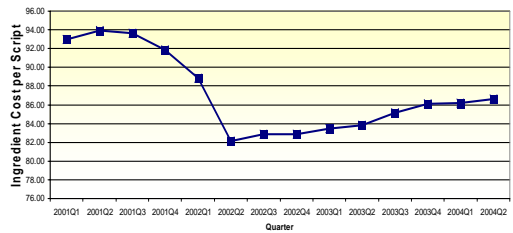
### Clinically-Informed Trend Analysis

#### Anti-depressants Market Share (Based on Scripts)



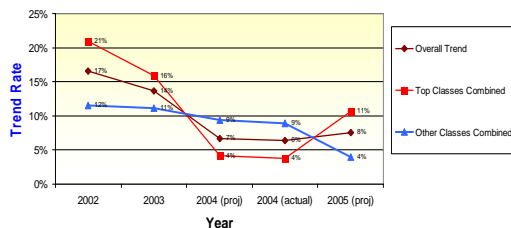
### Clinically-Informed Trend Analysis

#### Anti-depressants Ingredient Cost per Script (By Total Therapeutic Class)



### Clinically-Informed Trend Analysis

#### BCBS of Somewhere Pharmacy Trend History and Projections



Wrap Up

### **Wrap-Up**

- Clinically-Informed trend analysis requires detailed knowledge of what is going on in pharmacy
  - This knowledge helps you anticipate trends
  - This is “actionable” knowledge
- With Clinically-Informed trend analysis you can ultimately achieve targeted trends
  - You can implement clinical programs to react to trends more quickly
  - You can price, or budget, for your pharmacy costs more accurately

## **Accuracy is Money**