Specialty Pharmaceuticals: Market Overview

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Presentation Overview

• Defining Specialty Pharmacy
• Current and Future Trends in Specialty Pharmacy
• Coverage and Management of Specialty Pharmaceuticals
• Future Challenges
Defining Specialty Pharmacy
What Are Specialty Pharmaceuticals?

- A category of drugs resulting from advances in drug development research, technology, and design
- Target and treat specific chronic or genetic conditions typically with an unmet need for therapeutic intervention

**Specialty Pharmaceuticals Include**

- Biopharmaceuticals (bioengineered proteins)
- Blood-derived products
- Complex molecules
- Select oral, injectable, and infused medications

**Specialty Pharmaceuticals Require…**

- Tailored patient education for safe and effective use
- Patient specific dosing
- Monitoring for serious side effects
- Administration via injection, infusion or orally
## Current Biotech Diseases/Therapies and Related Drug Examples

<table>
<thead>
<tr>
<th>Disease/Therapy</th>
<th>Drug Name</th>
<th>Disease/Therapy</th>
<th>Drug Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td><em>Xolair</em></td>
<td>Multiple Sclerosis</td>
<td><em>Avonex, Betaseron</em></td>
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<td></td>
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<td></td>
<td><em>Copaxone, Rebif, Tysabri</em></td>
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<tr>
<td>Anemias (Hematopoietics)</td>
<td><em>Procrit, Epogen, Aranesp, Neupogen</em></td>
<td>Pulmonary HTN</td>
<td><em>Remodulen</em></td>
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<td><em>Flolan</em></td>
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<td><em>Tracleer</em></td>
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<td>Crohn’s Disease</td>
<td><em>Remicade, Humira</em></td>
<td>Psoriasis</td>
<td><em>Amevive</em></td>
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<td></td>
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<td><em>Raptiva</em></td>
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<tr>
<td>Gaucher’s Disease</td>
<td><em>Cerezyme</em></td>
<td>Oncology</td>
<td><em>Rituxan</em></td>
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<td></td>
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<td></td>
<td><em>Gleevec</em></td>
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<td><em>Herceptin</em></td>
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<td></td>
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<td><em>Avastin</em></td>
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<td></td>
<td></td>
<td></td>
<td><em>Tarceva</em></td>
</tr>
<tr>
<td>Hemophilia</td>
<td><em>Recombinate, Benefix, other Factor products</em></td>
<td>Rheumatoid Arthritis</td>
<td><em>Enbrel</em></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td><em>Humira</em></td>
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<tr>
<td></td>
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<td></td>
<td><em>Remicade</em></td>
</tr>
<tr>
<td>Hepatitis C</td>
<td><em>Pegasys Peg-Intron</em></td>
<td>Growth Hormone</td>
<td><em>Nutropin</em></td>
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<tr>
<td></td>
<td></td>
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<td><em>Genotropin</em></td>
</tr>
<tr>
<td>Infertility</td>
<td><em>Gonal-F. Follistim</em></td>
<td>RSV</td>
<td><em>Synagis</em></td>
</tr>
</tbody>
</table>
## High Cost Specialty Therapies: Monthly and Annual Costs

<table>
<thead>
<tr>
<th>Disease State</th>
<th>Average Monthly Drug Cost Per Patient</th>
<th>Avg. Annual Drug Cost per Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemophilia</td>
<td>$20,000++</td>
<td>$240,000++</td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td>$3,600</td>
<td>$43,200</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>$1,600</td>
<td>$19,200</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>$1,650</td>
<td>$19,800</td>
</tr>
<tr>
<td>Rh. Arthritis</td>
<td>$1,400</td>
<td>$16,800</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>$1,400</td>
<td>$16,800</td>
</tr>
</tbody>
</table>
Specialty Pharmacy Trends
Key Drivers of Specialty Trend

High cost per patient

• Accounts for 15% of pharmaceutical spending in the US
• Annual growth at 15-20%
• Annual drug cost ranges from $15,000 - $250,000+ per patient
• Manufacturer price increases for existing drugs
• No generics available as products mature

Increasing utilization

• Flourishing pipeline
• Multiple indications for existing drugs
• Earlier use of biologics in treatment
• Move from rare diseases to more common chronic diseases
• Episodic vs. chronic treatment
Specialty Pharmacy Trend Rate Outpaces Traditional Drugs

Specialty vs. Non-Specialty Drug Trend
Year to Year % Increase in Drug Cost

Sources: Medco Drug Trend Report 2007, Express Scripts 2006
Pipeline View by Therapy Class

Biotech Drugs in Development

Transplant 4
Growth 4
Eye 6
Skin 7
Genetic 9
Blood 10
Respiratory 13
Gastrointestinal 14
Diabetes 15
Neurologic 17
Other 18
Cardiovascular 22
AIDS/HIV 22
Autoimmune 44
Infectious Disease 50
Cancer 210

418 in late stage development

Source: PhRMA 2006 Report: Medicines in Development
Biotechnology Pipeline
New Molecular Entities and Supplemental Indications
in Phase III Development

Caremark RxPipeline. September 2007 and March 2008

125% increase

2009-2011 projected trend = 20% annually

Express Scripts 2007 Drug Trend Report
Coverage and Management of Specialty Pharmaceuticals
Impact of Specialty Injectables

- High cost biotechnology drugs are changing the managed care “paradigm”
  - Traditional drug management strategies are not enough
  - “Siloed” drug management mentality not applicable

- Specialty drugs have been the fastest growing segment of drug spend

- SpRx represents significant challenges for private and public payers
  - Cost Management
    - Network
    - Patient Cost Share
  - Clinical Management
  - Utilization Management
  - Benefit Design
    - Is it Pharmacy or is it Medical?
Three Types of Specialty Drugs

**Rx Benefit**

Self-Administered Drugs
- RA: Enbrel, Humira, Kineret
- MS: Betaseron, Avonex, Copaxone, Rebif
- Growth Hormone
- Psoriasis: Enbrel, Raptiva
- Blood Modifiers: Epogen, Neupogen, Aranesp
- Cancer: Oral Oncolytics

**Med. Benefit**

Office Administered Drugs
- RA: Remicade, Ocrenica, Rituxan
- MS: Avonex, Growth Hormone
- Psoriasis: Amevive
- Blood Modifiers: Epogen, Neupogen, Aranesp, Procrit
- Asthma: Xolair
- Cancer: Infused Oncolytics

**Rx or Med Benefit**

Home Infused Drugs
- Hemophilia: Various
- Gaucher’s Disease: Cerezyme
- Fabry’s Disease: Fabrazyme
- PAH: Flolan, Remodulen
- IVIG

Some Crossover Occurs Between Sites of Administration
There Are Many Distribution Channels for Specialty Drugs

Each channel may receive a different reimbursement and be subject to different management practices.
Specialty Pharmacy Providers (SPP)

Owned by PBMs, health plan, drug chains, wholesalers, home infusion companies

Pharma trend to limit distribution of SpRX to select SPPs and restrict access

Clinical Services

Distribution

Reimbursement
Voluntary vs Mandatory Use of SPP

- HMO: Voluntary 35%, Some mandatory 28%, Mandatory 37%
- PPO: Voluntary 42%, Some mandatory 19%, Mandatory 39%
- MA-PD Part D: Voluntary 66%, Some mandatory 14%, Mandatory 20%
- Medicaid: Voluntary 28%, Some mandatory 28%, Mandatory 44%
- HMO: Voluntary 63%, Some mandatory 23%, Mandatory 14%
- PPO: Voluntary 63%, Some mandatory 23%, Mandatory 14%
- MA-PD Part B: Voluntary 75%, Some mandatory 18%, Mandatory 7%
- Medicaid: Voluntary 45%, Some mandatory 32%, Mandatory 23%

*EMD Serono Injectables Digest™ 4th Edition*
Over 50% of health plans allow patients to obtain self administered injectables through retail and SPP.
Over 60% of health plans that contract with SPPs allow physicians to continue to “buy and bill”
Specialty Pharmacy Therapy Management of Hepatitis C

Outbound Pt Call – Enrollment and Education

Outbound Pt Call – Initiate Discussion Following First Dose: Discuss ADRs, Adherence, Response; Schedule Next Refill

Outbound Pt Calls – Discuss ADRs, Adherence, Response; Initiate Discussion and Schedule Next Refill

Outbound Pt Call – Follow up to Therapy, Assess Outcomes

Patient Starter Packet

Monitor Early Virologic Response

Assess for Early Responder
Clinical and Utilization Management
Payers Want to Ensure Appropriate Utilization

**Right Drug**

Is this the correct dose?

Is this the right time in the regimen?

Does the pt. have enough meds? Too many?

**Right Drug**

Is there another medication that may be more appropriate?

Or may be less expensive yet equally effective?

**Right Time**

Should therapy be discontinued?

Have labs been performed at the right time to measure results?

**Right Patient**
Payers Employ a Variety of Utilization Management Techniques

- Development of clinical guidelines and criteria
- Prior authorization to ensure appropriate use
- Step therapy guidelines
- Promote formulary with preferred products
- Reduce waste and over-use
Managing Specialty Therapies: Identifying the Patient

Psoriasis-Example

General Population
1,000

Patients with Psoriasis
26

Patients with Moderate to Severe Disease
6.5

Patients at Highest Risk and Target for New Agents
1.6

Conventional Options
Topical Therapies, Phototherapy
Systemic Medications

Biotechnology Options
Biotechnology Products

Specialty Guideline Management
Condition Specific Case Study – RSV

--- | --- | --- | --- | --- | ---
Did not meet AAP Guidelines | 23% | 28% | 28% | 36% | 38%
Number of Doses Avoided | 1,300 | 1,287 | 941 | 1,278 | 1,391
Cost Avoidance | $ 1.9M | $ 1.9M | $ 1.5M | $2.1M | $2.5M

Source: Caremark Analytics and Outcomes analysis.
Benefit Design Issues
Misaligned Financial Incentives Among Stakeholders

**Patient**
- I want the lowest copay

**Specialty Pharmacy**
- I want the highest reimbursement

**Doctor**
- I want to make a profit on the drug
Payers are Looking at New Benefit Strategies to Manage Specialty Drugs

Changing Benefit Design
- Trend to move from Medical Benefit to RX Benefit
- New Specialty Benefit
- Results in equalizing cost sharing, deductibles, clinical review

Increased Pt. Cost Share
- Creation of 4th copay tier
  - % coinsurance/higher flat copay
- Out-of-pocket maximums per RX
- Deductibles
- Annual or lifetime maximum benefit

Payers face an ethical dilemma — how much copay is too much?
Looking to the Future
Payer Shifting Focus on Specialty

**Previous Expectations**
- Biologics were indicated for treating rare diseases only
- Payers implemented few management tactics
- Physicians were given “carte blanche” related to prescribing
- Some therapeutic categories viewed as “off-limits”
  - Oncology
  - HIV/AIDS
  - Genetic disorders

**New Expectations**
- Biologics will shift from treating rare disease to more common diseases
- No drug categories are “off-limits” if there is sufficient utilization and concern about their value and appropriate use
- New biologic treatments must result in favorable outcomes – both clinical and economic
- Shift burden of proof of overall value to pharma
- Develop a standardized approach to manage total specialty spend regardless of site or method of administration
- Physicians will be more accountable for their therapy selections and reimbursement will be equalized across channels
Focus on Outcomes

• Uncertainty Related to Outcomes
  – Safety, efficacy and cost concerns
    • 75 new or revised black box warnings in 2007
  – Outcomes data not available when a new drug comes to market
  – Efficacy varies across patient populations and indications
  – Payers demanding pharmacoeconomic value from new therapies
  – Many new therapies do not provide quantifiable outcomes
  – FDA accelerated approvals
    • Product approval for life threatening diseases available on the market on the basis of preliminary evidence prior to formal demonstration of patient benefit.
  – Pharma may be required to document outcomes via a Pay for Performance (P4P) model.
  – P4P’s intent is to improve evidence base for safety, comparative effectiveness and value
    • Move focus from EBM to outcome based medicine
    • Comparative effectiveness of competing agents
    • Improve value for money paid as well as quality of care
# Global P4P Models: Will This Work in the US?

<table>
<thead>
<tr>
<th>Type of Model</th>
<th>Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price/Volume</td>
<td>Payment is linked to predetermined utilization based on prevalence or sub-groups to limit budget impact and inappropriate use</td>
<td>55 agreements in Australia including anti-TNF and Spiriva. Other agreements in France and Italy.</td>
</tr>
</tbody>
</table>
| Performance or Risk-based | Different reimbursed price depending on patient outcomes                     | **NICE/UK**  
 Multiple sclerosis DMDs  
 Manufacturers at risk for cost if defined outcomes are not achieved  
 **Velcade (bortezomibe)**  
 Manufacturer refunds cost if target outcome not achieved |
Selecting Optimal Therapy

40-60% of patients do not benefit from the drugs they are prescribed

- Hyper Metabolizers
  - No Effect
- Extended Metabolizers
  - Desired Effect
- Poor Metabolizers
  - Adverse Effects
- Poor Responders
- High Responders
- Non Responders

Adapted from PWC Personalized Medicine 2005
# Examples

## Disease Treatment

<table>
<thead>
<tr>
<th>Disease</th>
<th>Drug</th>
<th>Mechanism</th>
<th>Diagnostic test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>Herceptin®</td>
<td>Inhibit HER2 receptor</td>
<td>IHC and FISH</td>
</tr>
<tr>
<td>CML &amp; Malignant gastrointestinal stromal tumors (GIST)</td>
<td>Gleevec®</td>
<td>Inhibits Bcr-Abl protein</td>
<td>BCR-ABL (CML), C-KIT (GIST)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Genetic test to monitor emergence of Gleevec resistance</td>
</tr>
<tr>
<td>Various solid tumors</td>
<td>Various</td>
<td>Identify resistance to chemotherapy and clinical failure or potential success</td>
<td>Oncotech EDR® Assay</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Various</td>
<td></td>
<td>Phenotypic and genotypic resistance testing</td>
</tr>
</tbody>
</table>

## Reduce Adverse Drug Reactions

<table>
<thead>
<tr>
<th>Marker</th>
<th>Drug</th>
<th>Mechanism</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytochrome P450 metabolism</td>
<td>30 different forms of CP450 coded by a different gene</td>
<td>Variations in genes lead to ↑ or ↓ in metabolism of drugs</td>
<td>Amplichip® detects variations in 2</td>
</tr>
<tr>
<td>Camptosar</td>
<td></td>
<td>Predict patient’s safety-related response</td>
<td>UGT1A1 assay</td>
</tr>
</tbody>
</table>

## Disease Prevention

<table>
<thead>
<tr>
<th>Disease</th>
<th>Genetic Variant</th>
<th>Indication</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast and Ovarian Cancer</td>
<td>BRCA1 and BRCA2</td>
<td>Indicates hereditary propensity for cancer</td>
<td>Guide preventive measures</td>
</tr>
</tbody>
</table>
Public Perception of Specialty Pharmaceuticals
Specialty Drug Costs are Viewed as a “Side Effect”

“Payers Aim to Rein in Specialty Drug Spending”
*Wall Street Journal 3/20/08*

**Side Effects**

The average cost of a monthly prescription is going up for many drug classes.

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Cost (2007)</th>
<th>Change from 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>$1816.38</td>
<td>15.8%</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>$1647.00</td>
<td>12.1%</td>
</tr>
<tr>
<td>Blood-cell deficiency</td>
<td>$1724.51</td>
<td>9.0%</td>
</tr>
<tr>
<td>Inflammatory conditions</td>
<td>$1547.97</td>
<td>4.6%</td>
</tr>
<tr>
<td>Growth-hormone deficiency</td>
<td>$2569.10</td>
<td>1.8%</td>
</tr>
</tbody>
</table>

Source: Express Scripts (prices are paid by the pharmacy-benefits manager)

2. Table reported in the Wall Street Journal, 3/20/2008.

- Current specialty drug spend is $60 billion
- Expected to reach $99 billion by 2010
- Annual trend rate is 15–20%
Specialty Pharmacies, Pharma and Health Plans Portrayed as “Pushing Prices Higher”

New York Times, 4/14/08

“Co-payments Soar for Drugs with High Prices”

Blames employers and plan sponsors for the high cost of biotech treatments.

New York Times, 4/19/08

“Paid to Control Drug Costs, Yet Pushing Some Prices Higher”

Blames high cost of biotech drugs on those who dispense and manage biotech products.

Focus on drugs with limited or exclusive distribution.
Issues to Consider…

• How private and public payers can continue to offer affordable benefits to all enrollees with increased use of biologics

• How to equitable adjust cost share for persons who need to take expensive biologics

• How to remove administrative decisions about benefit design and reimbursement when selecting the appropriate drug for the patient

• The lack of a viable biosimilar pathway

• How to monitor therapy adherence and outcomes that show effectiveness of therapy

• How to overcome data management challenges within the legacy medical claims system
Top specialty drug spend
Pharmacy benefit and medical benefit – 2006

Pharmacy

- Hep C: 4.6%
- Anemia: 5.1%
- Growth hormone: 6.5%
- Cancer: 15.5%
- Multiple sclerosis: 18.0%
- Rheumatoid arthritis: 25.2%
- All other: 25.1%

Medical

- Neutropenia: 14.5%
- Anemia: 16.6%
- Cancer: 31.3%
- Rheumatoid arthritis: 15.3%
- All other: 22.0%

Medco 2007 Drug Trend Report
Changing Cost and Prevalence in Biotechnology: Shift Toward Larger Target Populations

The old specialty model: high cost, low prevalence

Average annual cost per patient (thousands)

- Gaucher's disease
- Hemophilia
- Growth hormone deficiency
- RSV
- Autoimmune disorders
- MS
- Crohn's
- HIV/AIDS
- RA
- Cancer
- Plaque psoriasis
- HCV

Estimated prevalence

1 million


HCV=hepatitis C virus. MS=multiple sclerosis, RA=rheumatoid arthritis. RSV=respiratory syncytial virus.

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The Promise of Personalized Medicine

Better diagnoses and earlier interventions.
- Detect disease at earlier stage
- Reduce adverse drug reactions
- Shift emphasis from REACTION to PROACTION

More efficient drug development.
- Design targeted therapies based on molecular pathways
- Smaller defined patient population to reduce initial cost and duration of clinical trials
- Reduce time, cost and failure rate of clinical trials

More cost-effective therapies.
- Cost savings realized through proactive and preventive interventions
- More patients seeking care once identified
- Less patients requiring “shotgun” or ineffective therapy
- Select optimal therapy and reduce trial and error prescribing