Pharmacy Benefit Drug Trends and Pipeline
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Pharmacy Management

Disclosure and Conflict of Interest
Dr. Robinson declares no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings and honoraria.

Pharmacist Objectives
At the conclusion of this program, the pharmacist will be able to:
• 1. Discuss current pharmacy benefit spend and trends
• 2. Evaluate how pharmacy benefit spend is managed today
• 3. Recognize drugs in the FDA pipeline and where pharmacy benefit spend will be in the future
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• 1. Discuss current pharmacy benefit spend and trends
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Pre-test Questions

• True or False:
  – Pharmaceuticals make up 50% of total health care spend.

Pre-test Questions

• All of the following are characteristics of specialty drugs EXCEPT?
  A) Expensive
  B) Brand Name Only
  C) Require Close Monitoring
  D) Treat Complex Disease States

Pre-test Questions

• Payers implement what strategies to control costs?
  A) Adherence programs
  B) Formulary Positions
  C) Value Based Contracts
  D) B & C
  E) A, B, & C
Pre-Test Questions

- Biosimilars
  - A) are interchangeable with a branded product
  - B) require an NDA for approval
  - C) are highly similar to an FDA approved product
  - D) cost roughly 20% of the reference product

Pharmacy Benefit Drug Trends and Pipeline

CURRENT STATE OF SPEND

The Players in Managed Care Pharmacy
In 2015, US Health Care spending reached $3.2 Trillion
- 10% of overall spend was on prescription drugs
  - Other areas of spend:
    - Hospital Care: 32%
    - Physician/Clinical Services: 20%
- Spending on prescription drugs outpaced all other services
  - Prescription Drug Spend Trend
    - 2014: 12.4%
    - 2015: 9.0%
  - Hospital Care Trend
    - 2014: 4.6%
    - 2015: 5.6%
  - Physician/Clinical Services Trend
    - 2014: 4.8%
    - 2015: 6.3%

The Growth of Specialty Drugs
- What is a specialty drug?
  - There is no standard definition for a specialty medication, but drugs in this category typically share one or more of the following characteristics:
    - They are expensive
      - The average monthly cost to payers and patients for a specialty medication is $3,000, ten times the cost for non-specialty medications.
    - They can be difficult to administer
      - They are often given by injection or infusion to treat complex, chronic conditions such as rheumatoid arthritis, multiple sclerosis and psoriasis
    - The drugs may require special handling, including temperature control
    - Patients taking these medications may need ongoing clinical assessment to manage challenging side effects.

Current Top Therapeutic Classes by Spend
- Inflammatory Conditions
- Oncology
- Diabetes
- Multiple Sclerosis
- HIV
- Hepatitis C
- Asthma

Current Top Therapeutic Classes by Spend - Specialty
- Inflammatory Conditions
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- Asthma
Current Top Therapeutic Classes by Spend - Specialty

- Inflammatory Conditions
  - Humira, Enbrel, Stelara
- Oncology
  - Keytruda, Revlimid
- Diabetes
  - Glumetza, Tresiba, Toujeo, Lantus, Levenir
- Multiple Sclerosis
  - Tecfidera, Copaxone
- HIV
  - Truvada, Stribild
- Hepatitis C
  - Harvoni
- Asthma
  - Advair, Dulera

MANAGING SPEND

Tools Used by Payers to Control Costs

- Coverage Positions/Formulary Management
- Utilization Management
- Benefit Design
- Rebate Management
- Outcomes Based Contracts

Coverage Positions/Formulary Decisions

- Value Based Formularies
  - Tiering
  - Closed Periods
  - Exclusions of Egregiously Priced Drugs
  - “Lifestyle” exclusions
Utilization Management

- Prior Authorizations
- Step Therapy
- Case Management
  - $77 PMPY savings with integrated management
- Mandatory Generics

Plan Design

- High Deductible Health Plans
- Coinsurance vs Copays
- Value Based Incentive Care vs Affordable Care
- Limited Networks
- 340B Pricing Arrangements

Rebates

Controversial topic within drug pricing
Moneys paid by the manufacturer to a payer based on utilization

<table>
<thead>
<tr>
<th>Drug</th>
<th>IMS estimated U.S. price (SH)</th>
<th>Company reported U.S. price (SH)</th>
<th>Manufacturer rebate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipitor</td>
<td>$7.7</td>
<td>$5.1</td>
<td>32%</td>
</tr>
<tr>
<td>Novo</td>
<td>$0.8</td>
<td>$0.8</td>
<td>0%</td>
</tr>
<tr>
<td>Humira</td>
<td>$9.2</td>
<td>$2.4</td>
<td>75%</td>
</tr>
<tr>
<td>Dilaudid</td>
<td>$11.7</td>
<td>$3.1</td>
<td>72%</td>
</tr>
<tr>
<td>Sensipal</td>
<td>$1.4</td>
<td>$1.1</td>
<td>21%</td>
</tr>
<tr>
<td>Bicarbis</td>
<td>$4.0</td>
<td>$3.5</td>
<td>23%</td>
</tr>
<tr>
<td>Ctrados</td>
<td>$4.4</td>
<td>$2.1</td>
<td>50%</td>
</tr>
<tr>
<td>Cymbalta</td>
<td>$3.7</td>
<td>$0.2</td>
<td>14%</td>
</tr>
<tr>
<td>Primax</td>
<td>$9.0</td>
<td>$9.4</td>
<td>2%</td>
</tr>
</tbody>
</table>

Source: IMS Health, company statements, and/or reports

Outcomes Based Contracts

- “Put your money where your mouth is.”
- Contracts based on drug performance in real world
- Examples:
  - Hepatitis C
  - Diabetes
  - Heart Failure
WHAT IS COMING?

FDA Novel Drug Approvals

Growth of Orphan Drugs

FDA Approvals 1999-2016

FDA Approvals: 1999-2016
Biosimilars

• What is a biosimilar?
  – Biosimilars are a type of biological product that are licensed (approved) by FDA because they are highly similar to an already FDA-approved biological product, known as the biological reference product (reference product), and have been shown to have no clinically meaningful differences from the reference product.

• Potential cost savings avenue for biologic drugs

Approved Biosimilars

<table>
<thead>
<tr>
<th>Currently on Market</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enbrel, Granix (for Neupogen)</td>
<td>Granix (for Neupogen)</td>
</tr>
<tr>
<td>Inflectra (for Terisalica)</td>
<td>Similanta (for Terisalica)</td>
</tr>
<tr>
<td>Luspatercept MS 1701 (for Neovasc)</td>
<td>Berenice (for Epogen, Procrit)</td>
</tr>
</tbody>
</table>

Enbrel and Humira biosimilars are likely to see approval in late 2018.

Biosimilars

Timing | Affordability | Interchangeability
--- | --- | ---
• US Supreme Court decision between 180 day delay between 1st approval and market launch | • All currently marketed biosimilars are medical (e.g. IV administered) | • No biosimilar currently has interchangeable status, but our approach can be independent of status
• Patient challenges will still delay timing of market launch of several biosimilars | • All 2017 biosimilar launches are medical | • FDA has draft guidance for interchangeability
• AIO-based pricing and reimbursement for medical injectables causes delay in potential cost savings | • Pharmacy benefit managers can reflect cost discounts at launch | • Includes requirements for switching studies

New “Heavy Hitters” in Pipeline

• Dyslipidemia
• Migraine
• NASH
Dyslipidemia Key Market Events

<table>
<thead>
<tr>
<th>Timing</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/2016</td>
<td>Generic Creator launch</td>
</tr>
<tr>
<td>1/2011</td>
<td>Lemonade meta-launch</td>
</tr>
<tr>
<td>2/2017</td>
<td>Aegeri (Repaglinide) using Repaglinide + Sulfonyl (Plumbic) for patient enrichment. Medistar Court issued injunction preventing Regenomic from continuing to sell Plumbic until 2020, but puts injunction on hold pending appeal. Impact opposes court ruling coming in 2/2017</td>
</tr>
<tr>
<td>9/2017</td>
<td>Depuyka //128,881 il trumall trial results published</td>
</tr>
<tr>
<td></td>
<td>Study population (n=17,841) consisting ABGC (i.e. chronic kidney population)</td>
</tr>
<tr>
<td></td>
<td>Key endpoint (28 month), cardiovascular death/myocardial infarction/stroke</td>
</tr>
<tr>
<td></td>
<td>Shrink 9% vs. 8.1% in key endpoint 7%</td>
</tr>
<tr>
<td></td>
<td>2% absolute risk reduction (ARR)</td>
</tr>
<tr>
<td></td>
<td>5%6.4% IRR (metformin 21 IRR - 10mg/kg)</td>
</tr>
<tr>
<td></td>
<td>No difference in rates of cardiovascular death</td>
</tr>
<tr>
<td></td>
<td>Aegeri announces additional contracting options</td>
</tr>
<tr>
<td>1Q 2018</td>
<td>Aegeri: Vytorin (combination of \textit{Astra \&amp;} simvastatin) launch</td>
</tr>
<tr>
<td>1Q 2018</td>
<td>Completion of Plumbic QUEENIE outcomes trial</td>
</tr>
</tbody>
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Migraine Market Dynamics

- Estimated 12% of US populations have chronic migraines
- Current treatment:
  - Acute migraine: Triptans (e.g. Imitrex) are 1\textsuperscript{st} line treatment
  - Generalized, base drug class
  - Dosage forms include oral, injection, nasal
  - Prevention of migraine: Other drugs such as Beta-blockers, anticonvulsants, antidepressants, Botox
  - Botox: $6K-10K per year
- Pipeline → Shift to specialty
  - Calcium Gene-Related Peptide (CGRP) is a neurotransmitter
  - CGRP is thought to be a key trigger of migraine attacks
  - Reduced the number of migraines per month by about 50%
- Rx benefit; SC injection once monthly
- Cost estimated to be $8K-20K per year; $3-4B market in 2022

CGRP receptor antagonist monoclonal antibody pipeline

<table>
<thead>
<tr>
<th>Brandname (generic, formulation)</th>
<th>TEV 49125 (Tevo)</th>
<th>Galcanezumab (Tebo)</th>
<th>Eptinezumab (Nulo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1/2/3</td>
<td>II</td>
<td>II II/III</td>
<td>II</td>
</tr>
<tr>
<td>2022 US Sales (M)</td>
<td>642</td>
<td>817</td>
<td>91</td>
</tr>
</tbody>
</table>

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Migraine Spend Outlook

- Preliminary comments by 3 judges favor Regenomic. Regenomic could be the sole player on the market if Regenomic wins.
- 1Q 2018 | Plumbic OEPQFY outcomes trial results |
  - Formulated in 88% to 96% Blink only better than seen in Regenomic FOURNER.
- 1Q 2018 | FDA decision on acetaminophin (Abbott), 1\textsuperscript{st} CTP inhibitor |
  - Low, 2023 forecast is 7.7% at BTER/50 |
- 1Q 2018 | FDA decision on cilastatin (Akeawa), 1\textsuperscript{st} ApCDI inhibitor |
  - Low, 2027 forecast is 4.1% at BTER/50 |
- 1Q 2018 | Update to AIA/AHA/ASH guidelines and \textsuperscript{1} |
  - IBD
NASH Market Outlook

What is NASH?
- Form of nonalcoholic fatty liver disease (NAFLD) that can progress to cirrhosis, liver failure, and cancer
  - Like hepatitis C, no symptoms until advanced disease
  - Projected to be leading cause of liver transplants by 2020
- Both NAFLD and NASH are linked to obesity and diabetes
- US prevalence is estimated at 2.5%
  - ICER report projects 567,000 candidates for treatment
  - Cigna total population estimated at 20,000-30,000
- Diagnosis confirmed with liver biopsy
  - Goal of treatment → prevent fibrosis → prevent cirrhosis
  - Cost: Ocaliva is currently over $69,000 per year
  - Indication-based pricing opportunity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Timing</th>
<th>Mechanism of Action</th>
<th>Route</th>
<th>2022 US Sales (SM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obeticholic acid (Intercept®)</td>
<td>2017</td>
<td>Decreased receptor agonist</td>
<td>Oral</td>
<td>$867</td>
</tr>
<tr>
<td>Elafibranor (Comprid®)</td>
<td>2019</td>
<td>Decreased receptor agonist</td>
<td>Oral</td>
<td>NA</td>
</tr>
<tr>
<td>Setinobrevin (Civano)</td>
<td>2025</td>
<td>Decreased receptor agonist</td>
<td>Oral</td>
<td>1.6</td>
</tr>
<tr>
<td>Colestiblar (Mirage®)</td>
<td>2021</td>
<td>Cholesterol receptor 2, 5 antagonist</td>
<td>Oral</td>
<td>NA</td>
</tr>
</tbody>
</table>

What is gene therapy?

- A novel approach to treat, cure, or ultimately prevent disease by changing the expression of a person’s genes

How does gene therapy work?

- Voretigene (SPK-RPE65) for Leber’s congenital amaurosis
  - Ultra-rare inherited retinal disease that causes 20% of childhood blindness
  - Estimate of 3,500 cases in US and EU5
Diseases Targeted by Gene Therapy

<table>
<thead>
<tr>
<th>Area</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>Lung, ovarian, glioblastotic brain cancer</td>
</tr>
<tr>
<td></td>
<td>Leukemia</td>
</tr>
<tr>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td></td>
<td>Malignoma</td>
</tr>
<tr>
<td>Neurological</td>
<td>Parkinson's disease</td>
</tr>
<tr>
<td></td>
<td>Epilepsy</td>
</tr>
<tr>
<td></td>
<td>Alzheimer's disease</td>
</tr>
<tr>
<td></td>
<td>Muscular dystrophy</td>
</tr>
<tr>
<td></td>
<td>Huntington's disease</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
</tr>
<tr>
<td></td>
<td>Hepatitis C</td>
</tr>
<tr>
<td></td>
<td>Hepatitis B</td>
</tr>
<tr>
<td></td>
<td>Hepatitis A</td>
</tr>
<tr>
<td></td>
<td>Poliomyelitis</td>
</tr>
<tr>
<td></td>
<td>Amyotrophic lateral sclerosis</td>
</tr>
<tr>
<td></td>
<td>Mitochondrial disorder</td>
</tr>
<tr>
<td></td>
<td>Mitochondrial DNA</td>
</tr>
</tbody>
</table>

Post Test: Question #1

• True or False:
  – Pharmaceuticals make up 50% of total health care spend.

  • Per CMS, drug spend made up 10% of total health care spend in 2015 and is continuing to rise faster than other areas.

Post Test: Question #2

• All of the following are characteristics of specialty drugs EXCEPT?
  A) Expensive
  B) Brand Name Only
  C) Require Close Monitoring
  D) Treat Complex Disease States

  There is no set definition for specialty, but the industry does not limit specialty drugs to brands only. (example: Generic Gleevec)

Post Test: Question #3

• Payers implement what strategies to control costs?
  A) Adherence programs
  B) Formulary Positions
  C) Value Based Contracts
  D) B & C
  E) A, B, & C

  Adherence programs actually increase dispensing of drugs, so that would increase costs. However, that isn’t necessarily a bad thing!
Post Test: Question #4

- Biosimilars
  - A) are interchangeable with a branded product
  - B) require an NDA for approval
  - C) are highly similar to an FDA approved product
  - D) cost roughly 20% of the reference product

Interchangeability does not exist for biosimilars and the reference product; an NDA is not required through the biosimilar approval pathway and costs are higher than 20% of the reference product. The biosimilar must show that it is "highly similar" to the reference product for FDA approval.

Take Home Points

- Drug spend is growing at a faster rate than other areas of spend in health care
- Managed Care partners use several different approaches to control costs
- The growth of specialty drugs within new disease states is impactful to the future of pharmacy spend

Speaker Contact Information

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