Session 70, Specialty Pharmacy Pipeline Update and Management Concepts for Gene and Cell Therapies
2019 Health Meeting

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A look at what will drive future drug costs...and many of our futures.
PHARMACY COSTS FROM AN EMPLOYER’S PERSPECTIVE

While employees equally contribute to payment of premiums...

Illustrative based on actual 3500 life Maxor group

...a minority of utilizers drive costs
SPECIALTY VS TRADITIONAL SPEND TREND

Specialty growth trending at 11.7% versus 1.8% for traditional

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<tbody>
<tr>
<td>Specialty per (IQVIA)</td>
<td>34.9%</td>
<td>38.0%</td>
<td>40.1%</td>
<td>43.1%</td>
<td>45.4%</td>
<td>45.8%</td>
</tr>
<tr>
<td>MaxorPlus</td>
<td>28%</td>
<td>30.3%</td>
<td>31.7%</td>
<td>35.5%</td>
<td>38.7%</td>
<td>40.1%</td>
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*Source: IQVIA, National Sales Perspectives April 2019. Note: Specialty definitions and payer mix vary.
PHARMA’S PIPELINE REMAINS ROBUST

Per www.biomedtracker.com accessed 06/03/2019

Investigational Phase III and Beyond Drug Count (Lead Indication)

- Non-Orphan: 66%
- Orphan: 34%
<table>
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<tr>
<th>Unique Drugs Approved</th>
<th>Currently in Phase 3</th>
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<tbody>
<tr>
<td>Hypertension (Systemic)</td>
<td>Alzheimer's Disease (AD)</td>
</tr>
<tr>
<td>Diabetes Mellitus, Type II</td>
<td>Rheumatoid Arthritis (RA)</td>
</tr>
<tr>
<td>HIV / AIDS</td>
<td>Parkinson's Disease (PD)</td>
</tr>
<tr>
<td>Asthma</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td>Dyslipidemia / Hypercholesterolemia</td>
<td>Pancreatic Cancer</td>
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Accessed Biomedtracker 10/9/2018 by Sorted in descending order of Unique drugs whose Lead Indication is within the listed disease state.
The road to an Alzheimer's cure is littered with failed travelers

Over 200 compounds from dozens of organizations have failed in their attempt to gain an Alzheimer’s indication.

Approval of a molecule that reverses Alzheimer’s would likely be the biggest revenue-generating molecule in history.
Many researchers are still on the road

- Estimated at $5.6B total investment to bring Alzheimer’s drug to market

- US Prevalence is currently 5.5 million people (14 million by 2050).

Despite just 9 approved drugs, the US Drug spend on Alzheimer’s was approximately $1B in 2017....and these drugs do not prevent, cure or reverse the disease

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6118094/
NONALCOHOLIC STEATOHEPATITIS (NASH) A $10B+ OPPORTUNITY?

NASH Drugs in Pipeline

- Phase 2: 10, 59%
- Phase 3: 7, 41%

*Investment research varies, with several market size estimates ranging from $8B - $24B of worldwide sales by 2025.
4X MORE PREVALENT THAN HEPATITIS C

NONALCOHOLIC STEATOHEPATITIS (NASH)

• Estimated to affect between 6-16 million Americans
• 3rd leading indication for liver transplantation in US
• Often reversible with diet and exercise
• Will significant co-morbidities of the disease introduce marketing challenges for new pharmacotherapies?
CYSTIC FIBROSIS

• More than 30,000 people are living with cystic fibrosis (more than 70,000 worldwide).
• Approximately 1,000 new cases of CF are diagnosed each year.
• More than 75 percent of people with CF are diagnosed by age 2.
• More than half of the CF population is age 18 or older.

Source: https://www.cff.org/What-is-CF/About-Cystic-Fibrosis/
Manifestations of Cystic Fibrosis

General
- Growth failure (malabsorption)
- Vitamin deficiency states
  (vitamins A, D, E, K)

Nose and sinuses
- Nasal polyps
- Sinusitis

Liver
- Hepatic steatosis
- Portal hypertension

Gallbladder
- Biliary cirrhosis
- Neonatal obstructive jaundice
- Cholelithiasis

Bone
- Hypertrophic osteoarthropathy
- Clubbing
- Arthritis
- Osteoporosis

Intestines
- Meconium ileus
- Meconium peritonitis
- Rectal prolapse
- Intussusception
- Volvulus
- Fibrosing colonopathy (strictures)
- Appendicitis
- Intestinal atresia
- Distal intestinal obstruction syndrome
- Inguinal hernia

Lungs
- Bronchiectasis
- Bronchitis
- Bronchiolitis
- Pneumonia
- Atelectasis
- Hemoptysis
- Pneumothorax
- Reactive airway disease
- Cor pulmonale
- Respiratory failure
- Mucoid impaction of the bronchi
- Allergic bronchopulmonary aspergillosis

Heart
- Right ventricular hypertrophy
- Pulmonary artery dilation

Spleen
- Hypersplenism

Stomach
- GERD

Pancreas
- Pancreatitis
- Insulin deficiency
- Symptomatic hyperglycemia
- Diabetes

Reproductive
- Infertility
  (aspermia, Absence of vas deferens)
- Amenorrhea
- Delayed puberty

Cystic Fibrosis – Moving from a terminal diagnosis to a chronic disease

Diagnosis was usually equated to short life spans with only drugs that treated the symptoms and sequelae of disease...

New disease modifying therapies, new technology and healthcare collaboration are changing the landscape...

We expect many pediatric CF patients today will now live into their 60s and beyond!
There are over 2,000 potential mutations to the CFTR gene; treatments in phase 3 today are expected to expand or introduce treatment options for most all patients.
Many forces at play will shape our future drug costs

**HHS / Regulatory action**
- PAP programs
- Rebate rule

**Market Behavior**
- Point of sale rebates
- Biosimilars

**Pipeline**
- Novel allergy Treatments
- Ingestible delivery systems
- “Combo” oncology therapy
- Cell-based and Gene Therapies
Gene and Cell Therapy Trends and Management
Rare Diseases / Orphan Drugs

• Rare Diseases\(^1\)
  - A condition affecting ≤ 200,000 people in the [United States]
  - A condition affecting less than 1 in 2,000 [European Union]
  - Approximately 7,000 rare diseases impacting ~25-30M Americans
  - “In the United States, only a few types of rare diseases are tracked when a person is diagnosed. These include certain infectious diseases, birth defects, and cancers. It also includes the diseases on state newborn screening tests. Because most rare diseases are not tracked, it is hard to determine the exact number of rare diseases or how many people are affected.”

• Orphan Drug Act (1983)
  - Passed to encourage the development of drugs for rare disorders
  - Created the prevalence definition (above), in situations where, “there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from the sale in the United States.”\(^2\)


Gene & Cell Therapies are Making Headlines

Novartis says SMA gene therapy is cost-effective at $4-5 mln per patient
Reuter’s Healthcare, 11/5/2018

FDA to Accelerate Gene, Cell Therapy Approvals
January 21, 2019
The FDA expects to receive some 200 new gene and cell therapy INDs in the next two years and plans to expedite their processing by hiring up to 50 extra staffers to handle review and other tasks. The agency also is considering new guidances focusing on regenerative therapies.
Centerwatch.com, 1/21/2019

Gene therapy for inherited blindness sets precedent: $850,000 price tag
WaPo, Carolyn Y. Johnson January 3, 2018
Gene Modifying Therapy vs. CAR T

**Gene Therapy**
- Gene Therapy involves the transferring of genetic material into a patient.
- The genetic material changes how protein(s) is/are produced by targeted cells.
- The result is the introduction, removal, or change in the content of a person’s genetic code to treat or cure the disease.
- Carriers/vectors transport the genetic material to the targeted cells.

**Cell Therapy**
- Cell therapy is the transfer of intact, live cells into a patient to help lessen or cure a disease. The cells may originate from the patient (autologous cells) or a donor (allogeneic cells).
- The type of cells administered depends on the treatment (e.g., pluripotent, multipotent, and primary).
- Chimeric Antigen Receptor (CAR) T-cell therapy modifies a patient’s own immune cells (T-cells), which attach to antigens on the surface of cancer cells.

## Currently Marketed Gene / Cell Products

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Company</th>
<th>Approval Date</th>
<th>Therapy Type</th>
<th>Indication</th>
<th>Treatment Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provenge</td>
<td>Dendreon Pharmaceuticals</td>
<td>April-2010</td>
<td>CAR T</td>
<td>Asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer</td>
<td>$63,000 per dose</td>
</tr>
<tr>
<td>Imlygic</td>
<td>Amgen</td>
<td>October-2015</td>
<td>Viral</td>
<td>Local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery</td>
<td>$150,000 annually ($6,000 every 2 weeks)</td>
</tr>
<tr>
<td>Kymriah</td>
<td>Novartis</td>
<td>August-2017</td>
<td>CAR T</td>
<td>Specific instances of B cell acute lymphoblastic leukemia</td>
<td>$570,000</td>
</tr>
<tr>
<td>Yescarta</td>
<td>Kite/Gilead</td>
<td>October-2017</td>
<td>CAR T</td>
<td>Relapsed or refractory large B-cell lymphoma</td>
<td>$450,000</td>
</tr>
<tr>
<td>Luxterna</td>
<td>Spark Therapeutics</td>
<td>December-2017</td>
<td>Gene</td>
<td>Leber congenital amaurosis or retinitis pigmentosa</td>
<td>$500,000 (per eye)</td>
</tr>
<tr>
<td>Zolgensma</td>
<td>Novartis</td>
<td>May-2019</td>
<td>Gene</td>
<td>Type 1 Spinal Muscular Atrophy</td>
<td>$2.1M</td>
</tr>
</tbody>
</table>
Robust Pipeline of Orphan Therapies

- Worldwide orphan drug sales are forecast to total $209 billion and growing at a rate of 11.1% from 2017 to 2022, more than twice the rate predicted for conventional drugs.
- The market for orphan drugs is anticipated to be 21.4% of worldwide prescription sales by 2022 (excluding generics).
- The worldwide pipeline includes over 1,100 therapies targeting over 60 rare conditions.
Why Payers Should Care

• Gene Therapies carry significant actuarial risk
  - Unknown and potentially volatile number of affected patients
  - Anticipated costs per treatment in the range of $500K to $5M
  - With durable therapies, treatment costs are all front-loaded, rather than over time for traditional medicine/therapies/claim costs
  - Benefit design and adverse selection
  - Type and time horizon of value will vary dramatically from disease state to disease state

• Internal inefficiencies in developing management plans for a small number of potential patients

• External inefficiencies in establishing treatment networks and contracting with manufacturers

Source: Improving Management of Gene and Cell Therapies: The Orphan Reinsurer and Benefit Manager (ORBM). Trusheim, M et. al. Pharmaceutical Executive, September 10, 2018
Recent Orphan Drug Strategy Project

**The goal**
Assess current membership and claims experience to forecast the cost of gene therapies over the next 3-5 years.

### Claims Analytics
Research gene tx pipeline and related ICD-10 codes

### Clinical Research
Clinical assessment of current rare disease treatment options & costs

### Modeling & Planning
Developed actuarial model to forecast growth in treatment costs and anticipated cost offsets

1. Analyze claims experience to quantify rare disease membership exposure and associated treatment costs
2. Clinical assessment of pipeline gene therapies (e.g., subpopulations, place in therapy)
3. Build a planning framework to prepare cost, benefit, and clinical management in advance of gene therapies
Recent Orphan Drug Strategy Project (Cont’d)

- **Medicare** includes estimates for the following disease states: Scleroderma, Amyotrophic lateral sclerosis (ALS), Huntington's disease, Alpha-1 antitrypsin deficiency, sickle cell Anaemia, and Spinal muscular atrophy.

- **Commercial** includes estimates for the following disease states: Cystic fibrosis, sickle cell Anaemia, Hemophilia A & B, Amyotrophic lateral sclerosis, Aromatic L-amino acid decarboxylase (AADC) deficiency, and Spinal Muscular Atrophy.
Orphan Reinsurer & Benefit Manager Concept

- Creating financing solutions for durable/potentially curative therapies with large, upfront costs whose benefits accrue over time

**Financial Challenges**

- Timing of claim payments
- Actuarial risk
- Therapeutic outcomes risk (e.g., durability, efficacy)

**Key Features**

- Consolidate risk—carve-out and pool risk
- Contracting and payment
- Care coordination services
- May be National or Regional in scope

Source:
Strategies need to deliver contracting efficiencies, quality patient care coordination and effective risk pooling across dozens of rare diseases
Payer and Pharma Strategies are Emerging

Biotech Proposes Paying for Pricey Drugs by Installment
Bluebird Bio develops plan to sell gene-replacement therapy with annual payments contingent on continued effectiveness (WSJ, Jan 15, 2019)
Outcomes-Based Risk-Sharing Agreements (OBRSA)

- **Potential payer benefits:**
  - Optimized resource utilization and patient outcomes
  - Competitive product offerings
  - Member retention and growth
  - Financial sustainability
  - Positive public relations
  - Move away from a rebate-based reimbursement model

- **Potential manufacturer benefits:**
  - Maintained or improved formulary access
  - Competitive differentiation and growth
  - Financial sustainability
  - Generation of real-world evidence of value
  - Move away from a rebate-based reimbursement model

Specialty costs continue to increase
Out of total healthcare spend, 30% is spent on drugs

Pharmacy Benefit
- 33% specialty
- 67% non-specialty

Medical Benefit
- 58% specialty
- 42% non-specialty

Out of total healthcare spend, 30% is spent on drugs.

Specialty drug spend under the medical benefit by site of care:
- 47% Hospital Outpatient
- 42% Specialty Pharmacy & Infusion
- 11% Physician Office

1-2% members with specialty conditions
$4.1K average monthly cost
1/2 new drug approvals

Milliman, Commercial Specialty Medication Research: 2016 Benchmark Projections
Program Results

Establish care and partnership

Ongoing support

Optimize connections

~2% higher adherence than retail pharmacies

Condition-specific Outcomes

• Hemophilia: 1.18% assay variance = $22.4M savings vs. industry standard

• Oncology
  – 81% first fill consult rate and VOC of 83
  – Split Fill savings of $2,500 per discontinued patient per year*

• Multiple Sclerosis
  – Order conversion increased 2.2%
  – 20 point NPS increase in 4 months

INFLAMMATORY
20% higher adherence
4% lower medical costs

HEP C
21% higher adherence
10% lower medical costs
Specialty medical management solution
A Comprehensive & flexible solution for specialty medications

Benefit Shift Savings
$6-9 PMPM*

More robust prior authorization controls
Better clinical management oversight
Standardized cost structures

Same site of care
Same provider
Same experience

HOSPITAL OUTPATIENT

2-3x more expensive
Move site of care
Collaborative clinical care team to support transition
Convenient & cost effective

HOME, CLINIC & INFUSION SUITE

Blood Modifier
22% shift
$90K annual savings*

Inflammatory
22% shift
$13K annual savings*

Immunoglobulin
39% shift
$20K annual savings*

* Annual savings based on historical data and may vary based on individual circumstances.
The growth of copay cards

Copay cards are significantly increasing in availability and use

Copay Card Programs

80% specialty drugs 50% traditional drugs

Copay Card Accumulator

$1,995 copay card

$5 member cost share

$5 deductible

$5 applied to out-of-pocket max

Preferred Copay Card Acceptance Program
Encourages use of preferred lower cost drugs by restricting copay cards

Copay Card Accumulator Adjustment Program
Removes copay card contributions as part of accumulator calculations

Variable Copay Design
Maximize payments from manufacturer copay assistance programs while reducing cost to the plan and limiting member impact

Total drug spend increase from 2007 to 2010 when coupons were offered on 23 drugs facing generic competition³

Additional healthcare cost due to copay/coupons for non-specialty drugs alone, over the next 10 years³

$700M → $2.7B

1. IMS; 2. Tuffs Center Study. New England Journal of Medicine

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