Coverage of Rare Disease Therapies in Medicaid and Medicare and the Impact on Patient Care

Jay Greissing, Dir. U.S. Government Relations and Policy
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Philadelphia, PA
Agenda

- Increased Scrutiny of Rare Disease Therapies
  - What is a Rare Disease?
    - Definition and Examples
    - Impact on the Patient: The Diagnostic Odyssey
    - The Orphan Drug Act
    - Subsequent Federal Rare Disease Policy
    - Market Breakdown of Diseases and Therapies
    - Development Programs Meeting Unmet Need or Improving the Standard of Care
  - Medicaid Coverage Challenges for Rare Disease Therapies and Potential Solutions
    - Current Law
    - Examples of Restrictive Coverage Policies
    - State Perspective
    - Medicaid Spend on Rare Disease Therapies in 2014
    - The EPIC Act
  - Medicare Coverage Challenges for Rare Disease Therapies and Potential Solutions
    - Medicare Coverage of Home Infusion Therapy
    - Medicare Home Infusion Site of Care Act
    - Challenges with Medicare Part D Formularies
  - Impact of CMS Rule on Line Extension Rebates
  - Conclusion
Increased Scrutiny of Rare Disease Therapies

Modify ODA incentives to reflect modern drug development

Strip orphan status at $1B in annual sales


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Rare Diseases

- mucopolysaccharidoses types and subtypes
- hemophilia and other bleeding disorders
- hereditary angioedema
- cystinosis
- alpha-1 antitrypsin deficiency
- primary immunodeficiency diseases
- cystic fibrosis
- short bowel syndrome
- Gaucher disease
- Fabry disease
- Pompe disease

< 200,000 individuals
Diagnostic Odyssey of the Rare Disease Patient

• **5:** Average years from onset of symptoms.

• **7:** Average number of physicians required.

• **72-89%:** The percent of rare disease patients and caregivers surveyed have reported feelings of depression, anxiety, and stress associated with the disorder.

Marty Luczak – adult onset X-linked adenoseneulokidakystrophy

• 20 years and $500,000 treating symptoms with surgical interventions and specialist visits.
• Correct diagnosis only came after niece's baby diagnosed through NBS.
Orphan Drug Act

MARKET EXCLUSIVITY (21 U.S.C. § 360cc(a))
- Seven years

TAX CREDIT (26 U.S.C. § 45C)
- 50% of qualified clinical testing expenses

ORPHAN DRUG GRANT PROGRAM (21 U.S.C. § 360ee)
- $17M for FY 2016
### Subsequent Incentives for Developing Rare Disease Therapies

#### Fees
- **Exclusion from annual branded pharmaceutical fee** *See* 26 U.S.C.S. § 4001 note prec.

#### 340B
- **Exclusion from new categories of DSH hospitals.** *See* 42 U.S.C.S. § 256b(e).

#### Medicaid
- **Limited Medicaid drug rebates for blood clotting factors to 17.1%.** *See* 42 U.S.C.S. § 1396r-8(c)(1)(B)(iii)(II)(aa).

#### Medicare
- **Special Part B reimbursement for blood clotting factors (add-on payment and transition year at AWP).** *See* 42 U.S.C.S. § 1395u(o)(5); 42 U.S.C.S. § 1395u(o)(1)(A)(ii).

#### PCORI
- **Rare disease advisory panels convened in each instance rare disease considered for CER.** *See* 42 U.S.C.S. § 1320e(d)(2)(B)(ii)(III); § 1320e(d)(4)(A)(iii).

#### PRVs
- **FDA awards transferable priority review vouchers to sponsors of qualifying “rare pediatric disease” applications.** *See* 21 U.S.C.S. § 360ff.
Current Breakdown of Marketed Rare Disease Therapies

- Cancer (90) 30%
- Infectious Disease (33) 11%
- Heritable Metabolic Disorders (28) 9%
- Heritable Blood and Immune Disorders (19) 6%
- Toxins (17) 6%
- Non-heritable blood disorders (17) 6%
- Heritable Disorders (10) 3%
- Non-heritable Kidney & Liver Disorders (9) 3%
- Autoimmune Disorders (9) 3%
- Other Heritable Disorders (6) 2%
- Non-heritable Disorders (5) 2%
- Organ Transplant Rejection (7) 2%
- Other non-heritable disorders (15) 5%
- Non-heritable CNS disorders (16) 5%
- Non-heritable Heart & Lung Disorders (11) 4%
- Other Heritable Disorders (6) 2%

388 Unique Marketed Therapies for 299 Rare Diseases (as of Jan. 15, 2016)
With 7,000 rare diseases lacking an FDA-approved treatment, there are hundreds of rare disease therapy development programs.

**Unmet Medical Need**
- Duchenne muscular dystrophy
- Niemann-Pick Type C
- Batten disease
- Sanfilippo syndrome A and B
- metachromatic leukodystrophy
- X-linked adrenoleukodystrophy
- Friedreich’s ataxia
- dystrophic epidermolysis bullosa
- X-linked myotubular myopathy
- Alagille syndrome
- acute neuromyelitis optica
- primary sclerosing cholangitis
- systemic lupus erythematosus
- Cooley’s anemia

**Improved Standard of Care**
- Pompe disease
- Fabry disease
- hemophilia A and B
- HAE
- cystic fibrosis
- Hurler syndrome
- Hunter syndrome
- primary biliary cirrhosis
- homozygous familial hypercholesterolemia
- alpha-1 antitrypsin deficiency
- homocystinuria
- cancer
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States must cover “medically necessary” covered outpatient drugs if its manufacturer has executed a Medicaid Drug Rebate agreement w/ CMS. See 42 U.S.C.S. §1396a(a)(54); §1396r-8(a)(1).

Examples of Coverage Restrictions

- **Cystinosis**: Clinically superior drug, non-preferred
- **HAE**: Forced off-label use
- **Cystic Fibrosis**: Denial
- **MPS syndromes and Gaucher disease**: Placement on Line 656 of the Prioritized List of Health Services
In Georgia, a “clinically superior” cystinosis agent is non-preferred.

- **FDA regulations:** “Orphan exclusivity” for the “same” drug approved for the “same” rare disease as a previously approved drug requires a demonstration that the drug is “clinically superior.”
  - Safer;
  - More effective; or
  - Provides a major contribution to patient care.
- FDA determined extended-release cysteamine bitartrate is “clinically superior” to cysteamine bitartrate, yet Georgia Medicaid patients must meet PA criteria to obtain it.
Examples of Coverage Restrictions

In Pennsylvania, the only modern FDA-approved treatment for prophylaxis treatment of HAE is non-preferred, forcing off-label use.

- Patient must receive diagnosis and prescription from an allergist or immunologist.
- Using clinical trial inclusion/exclusion criteria to further limit patient population – requirements that are **not limitations or recommendations on its use specified by FDA in the label** and without clinical basis:
  - Patient must be tested for HBV, HCV, and HIV, documented vaccination for HBV.
  - Documented history of more than one HAE attack per month requiring hospital Emergency Room intervention with an acute therapy.
  - **Exception for stabilized patients and physician override for medical necessity.**

Because the therapy is a human plasma derivative, the clinical trials section states that patients administered it tested negative for HBV, HCV, and HIV.

Clinical trials section states that patients enrolled in the study had history of at least two HAE attacks per month.
“[Three cystic fibrosis] patients all meet the eligibility criteria established by [FDA in the label]…[but] Arkansas officials have said the patients must prove their disease has failed to benefit from older, less expensive therapies, a policy doctors say contradicts treatment guidelines.”


“Arkansas Medicaid officials have reached a legal settlement…[that] would resolve the patients’ concerns that Arkansas could deny them or other patients the drug in the future.”

Examples of Coverage Restrictions

Prioritized List of Health Services:

- Section 1115 waiver from CMS (currently extended through July 2016).
- Oregon legislature has approved funding for up to line 476.

Listed FDA-approved therapies for Gaucher disease, MPS I, MPS II, MPS IV, and MPS VI at line 661.

2016

Expanded the class of covered therapies for metabolic disorders beyond alpha-1 antitrypsin deficiency and HAE to include therapies for Gaucher disease, MPS I, MPS II, MPS IV, and MPS VI listed at line 64, but also lists them at line 656.

E.g., For Hunter syndrome, because of its placement on the list, Oregon has only covered episodic and symptomatic interventions, such as surgeries, hospitalizations, diagnostic imaging, physical therapy, antibiotics, and nebulizers, rather than therapy that replaces the deficient enzyme.
State Perspective of its Obligation

- States are obligated to be good stewards of federal funds allocated to Medicaid.
  
  - States are required to maintain “methods and procedures” to “safeguard against unnecessary utilization” of Medicaid care and services. 42 U.S.C.S. § 1396a(a)(3)(A).
  
  - States must have utilization control policies to limit coverage to medically necessary care and services. See 42 C.F.R. § 456.3.
$5.7B spent by Medicaid on rare disease therapies in 2014, accounting for:

- **21%** of the total Medicaid prescription drug spend in 2014; and
- **1.1%** of overall Medicaid spend in 2014.

Therapies approved for HAE accounted for 0.3% of the Medicaid prescription drug spend and 0.02% of the total Medicaid spend in 2014.
The EPIC Act Pursued by 140 Patient Organizations
**Equity for Patients through Individualized Care Act**

- **E**quity for individuals with rare diseases and conditions;
- **P**hysician and patient treatment determination;
- **I**nnovation of and access to individualized treatment; and
- **C**ontinuity of care.

Prohibits Medicaid and CHIP from requiring a prerequisite drug, test or other service (such as emergency room intervention), or placing any other restriction related to the use or prescribing of a covered outpatient drug that is prescribed for a rare disease or condition that is an FDA approved use of such drug.

Prohibits the use of section 1115 Medicaid demonstration project waivers to deny, restrict, or otherwise limit access to a covered outpatient drug that is prescribed for a rare disease or condition that is an FDA approved use of such drug.
Measuring and Communicating the Value of Rare Disease Therapies

- **Dilemma for state Medicaid agencies with limited budgets.**
  - Short-term budget discipline vs. long-term investment

- **Value difficult to quantify**
  - Limited data on economic burden of rare diseases
  - Limited health outcomes data quantifying the economic benefit of diagnosis and treatment of a rare disease.

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### Diagnosis and treatment of PIDD

Diagnosis and treatment of PIDD patients (excluding SCID) saves $80,000 per patient per year.

### MPS I

- Early diagnosis and initiation of treatment prior to the onset of symptoms in patients with attenuated MPS I can slow or prevent the development of severe clinical manifestations.

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# Jeffrey Modell Foundation, Economic Impact Study: Comparing Undiagnosed and Diagnosed Patients with Primary Immunodeficiency Diseases (2007)

$ N. Al-Sanna et al., Early Treatment with Laronidase Improves Clinical Outcomes in Patients with Attenuated MPS I: A Retrospective Case Series Analysis of Nine Sibships, Orphanet J. of Rare Diseases (2015)
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Medicare Coverage of Home Infusion Therapy

- Medicare Part B
  - Drugs infused w/ DME
  - Parenteral nutrition
  - IVIG for PIDD (does not cover nursing services, supplies, or equipment)

- Medicare Part D
  - Covers drugs, but not nursing services, supplies, or equipment.
  - Restrictive formularies can limit whether the drug is covered.
S. 275; H.R. 605

Covers the drug (including DME infused drugs currently covered by Part B) under Part D.

Covers nursing services, equipment, and supplies under Part B.

Requires prior authorization process to be “expeditious” to allow “meaningful access”

Stakeholder Feedback

- Concern with restrictive formularies and utilization management tools in Part D:
  1. Preserve existing benefit for DME infused drugs in Part B and exclude them from the Durable Medical Equipment, Prosthetics, Orthotics and Supplies Competitive Bidding Program.
  2. Provide coverage for all other rare disease therapies in Part B unless such drugs are designated as a Part D “protected class.”

- Additional coverage: Coverage of “training, education, and monitoring services”
Concerns with Rare Disease Therapy Coverage in Part D

Medicare Model Guidelines fail to provide an adequate drug coverage “floor” for patients with rare diseases.

Current law requires Part D plans to offer a **minimum of 2 drugs** per USP category or class.

Enzyme Replacement/Modifiers USP drug category include 12 different inborn errors of metabolism.

**All diseases w/ unique pathophysiology and clinical manifestation**

- congenital sucrase-isomaltase deficiency
- cystinosis
- Fabry disease
- Gaucher disease
- hereditary tyrosinemia type 1
- homocystinuria
- MPS type I (Hurler, Hurler-Scheie, and Scheie syndromes)
- MPS type II (Hunter syndrome)
- MPS type VI (Maroteaux-Lamy syndrome)
- Phenylketonuria
- severe combined immunodeficiency associated with ADA deficiency
- urea cycle disorders

More than 20 drugs w/ different mechanisms of action
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Proposed Rule

- Conflicts with the Sherman Act (Antitrust)
- Conflicts with efforts to curb prescription drug abuse
- Conflicts with NIH and FDA repurposing
- Conflicts with Orphan Drug Act
- Conflicts with 30 years of rare disease policy

Final Rule

- CMS did **not** finalize the definition of “line extension,” including the use of the FDA Chemical Type system, and are accepting additional comments by April 1, 2016.

- CMS will **not** treat a drug as a “line extension” if the initial brand drug is manufactured by a **different** company **unless** there is a “corporate relationship” between the two manufacturers.
CMS explicitly includes drugs with orphan exclusive approval.

- More than a “slight alteration”: A “line extension” that has received orphan exclusive approval for the same indication as the initial brand, however, would have had to demonstrate it is “clinically superior,” which means FDA has determined it “provide[s] a significant therapeutic advantage over and above that provided by [the initial brand]” in terms of safety, efficacy, or by making a major contribution to patient care.

E.g., FDA determined Raptor’s Procysbi (cysteamine bitartrate (delayed release capsules)) is “clinically superior” to Mylan’s Cystagon (cysteamine bitartrate (immediate release capsules)) for treating cystinosis.
## Medicaid Line Extension Rebates

<table>
<thead>
<tr>
<th>Line Ext.</th>
<th>Rare Disease</th>
<th>Dosage Form</th>
<th>Initial Brand</th>
<th>Indication(s)</th>
<th>Dosage Form</th>
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<tbody>
<tr>
<td><strong>Abilify</strong></td>
<td>Tourette's disorder</td>
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<td>Abilify</td>
<td>Tourette's disorder, schizophrenia, bipolar, major depressive disorder, autistic disorder</td>
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<td>(disintegrating)</td>
<td>Otsuka</td>
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<td><strong>Adcirca</strong></td>
<td>Pulmonary arterial hypertension</td>
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<td>Cialis</td>
<td>Erectile dysfunction; benign prostatic hyperplasia</td>
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<td>(tadalafil)</td>
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<td>(Type 1; NME)</td>
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<td>Lung Biotechnology</td>
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<td>Lilly</td>
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<td><strong>Afinitor</strong></td>
<td>Subependymal giant cell astrocytoma with tuberous</td>
<td>tablet (suspension)</td>
<td>Afinitor</td>
<td>Subependymal giant cell astrocytoma with tuberous sclerosis complex; progressive neuroendocrine tumors of pancreatic origin; renal cell carcinoma, renal angiomyolipoma and tuberous sclerosis; breast cancer</td>
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<td>Disperz</td>
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<td>sclerosis complex</td>
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<td>not orphan designated</td>
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**Type 3**: New Dosage Form  
**Type 1**: NME  
**Type 6**: New Indication  
**NME**: New Molecular Entity  
** orphan designated**: Not designated as orphan  
**orphan exclusivity ends**: Date when orphan exclusivity ends
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<tr>
<td>Astagraf XL (tacrolimus) (Type 3; New Dosage Form)</td>
<td>kidney transplants&lt;br&gt;No orphan exclusivity</td>
<td>capsule (extended release)</td>
<td>Prograf (tacrolimus)&lt;br&gt;(Type 1; NME)</td>
<td>kidney, liver, and heart transplants</td>
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<td>Evista (raloxifene hydrochloride) (Type 6; New Indication)</td>
<td>breast cancer&lt;br&gt;(reduction in risk in women with osteoporosis or at high risk)&lt;br&gt;(orphan exclusivity ended 09/13/2014)</td>
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<td>Lennox-Gastaut syndrome&lt;br&gt;(orphan exclusivity ended 08/24/2005)</td>
<td>tablet (chewable)</td>
<td>Lamictal (lamotrigine)&lt;br&gt;(Type 1; NME)&lt;br&gt;GSK</td>
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<td>Zortress (everolimus)</td>
<td>kidney transplant; liver transplant</td>
<td>tablet</td>
<td>Afinitor (everolimus)</td>
<td>subependymal giant cell astrocytoma with tuberous sclerosis complex; progressive neuroendocrine tumors of pancreatic origin; renal cell carcinoma, renal angiomyolipoma and tuberous sclerosis; breast cancer</td>
<td>tablet</td>
</tr>
<tr>
<td>(Type 5; New Formulation or Manufacturer)</td>
<td></td>
<td></td>
<td>Novartis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Novartis</td>
<td>No orphan exclusivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urso 250/ Forte (ursodiol)</td>
<td>primary biliary cirrhosis</td>
<td>tablet</td>
<td>Actigall (ursodiol)</td>
<td>gallbladder stones</td>
<td>capsule</td>
</tr>
<tr>
<td>(Type 3; New Dosage Form)</td>
<td>(orphan exclusivity ended 12/10/2004)</td>
<td></td>
<td>Actavis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actavis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xifaxan (rifaximin)</td>
<td>hepatic encephalopathy</td>
<td>tablet</td>
<td>Xifaxan (rifaximin)</td>
<td>travelers' diarrhea</td>
<td>tablet</td>
</tr>
<tr>
<td>(Type 6; New Indication)</td>
<td>(orphan exclusivity ends 03/24/2017)</td>
<td></td>
<td>Salix</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salix</td>
<td></td>
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</table>
Increased Scrutiny of Rare Disease Therapies

What is a Rare Disease?
- Definition and Examples
- Impact on the Patient: The Diagnostic Odyssey
- The Orphan Drug Act
- Subsequent Federal Rare Disease Policy
- Market Breakdown of Diseases and Therapies
- Development Programs Meeting Unmet Need or Improving the Standard of Care

Medicaid Coverage Challenges for Rare Disease Therapies and Potential Solutions
- Current Law
- Examples of Restrictive Coverage Policies
- State Perspective
- Medicaid Spend on Rare Disease Therapies in 2014
- The EPIC Act

Medicare Coverage Challenges for Rare Disease Therapies and Potential Solutions
- Medicare Coverage of Home Infusion Therapy
- Medicare Home Infusion Site of Care Act
- Challenges with Medicare Part D Formularies

Impact of CMS Rule on Line Extension Rebates

Conclusion
• Generally, rare disease therapies benefiting the patient by satisfying unmet need or improving the standard of care are covered with limited issue in Medicaid and Medicare.

• Some rare disease therapies that provide high value to the patient and the health care system, however, are beginning to experience significant challenges in Medicaid and Medicare – is this the beginning of a trend, or more of an anomaly?

• Rare disease therapies are not well suited for traditional utilization management tools being employed, which are having a negative impact on patients.

• With increased scrutiny of rare disease therapies and evolution of precision medicine, industry must articulate the long-term benefit of early diagnosis and treatment to both the patient and the health care system.
QUESTIONS?