Rare Diseases and the Orphan Drug Act

Center Forward Basics

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Overview

With the **Orphan Drug Act (ODA)** entering its forty-first year in 2024, advocates and lawmakers are taking stock of the United States' progress in treating patients with rare diseases. Today, patients with rare diseases have shorter diagnostic journeys and more viable treatments than ever before. Despite this progress, hurdles continue as the gap between conditions and treatments remains large, and the power of the ODA has decreased over time. Lawmakers and experts are searching for solutions that will align incentives, improve the supply chain, and foster an ecosystem that will provide more options for patients. In this Basic, we will give an overview of the ODA, its impact, how it has changed over time, and what changes could be made in the future.

Rare Diseases and the ODA

Rare diseases are conditions that affect less than 200,000 Americans. While labeled "rare," these conditions become quite prevalent in aggregate. Some estimates find there are somewhere between 7,000 to 10,000 identified "rare" diseases, affecting more than 30,000,000 Americans. However, the comparatively small number of people suffering from each disease makes investing in treatments less attractive for financial investment. In response to this problem, Congress passed the Orphan Drug Act (ODA) in 1983. The ODA provides financial incentives to attract investment towards rare disease treatments. In this respect, the United States is unique and has been at the cutting-edge of rare disease science for decades. Initially, the legislation offered seven years of market exclusivity regardless of patent status and tax credits of up to 50% for research and development. These provisions made research and development for rare conditions financially viable, bringing new treatments to market.

Success of the ODA

Overwhelming evidence suggests the ODA has successfully facilitated the production of treatments for rare diseases and getting those treatments to patients. Before 1983, the Food and Drug Administration (FDA) approved 38 drugs to treat rare diseases. From 1983 to 2022, the FDA granted 1,122 approvals to treat rare diseases. The amount of rare disease drug development has continued to increase over time, as the last decade has seen nearly seven times as many designations as the first decade after the ODA's enactment. Developing rare disease treatments is an iterative process. The technology and science used to develop treatment for one disease often opens the door for developing novel treatments to other diseases in related areas. This gives each dollar invested in rare disease research a compounding effect that helps develop treatments for both rare and common illnesses.

Pharmaceutical development resulting from the ODA has changed the way doctors and patients think about some conditions from untreatable to manageable. Cystic Fibrosis (CF) is a genetic disorder that damages the lungs, digestive system, and other organs. Patients with CF have mutations in their cells that produce mucus, causing thick and sticky mucus to block

Center Forward Basics

Center Forward brings together members of Congress, not-for profits, academic experts, trade associations, corporations and unions to find common ground. Our mission: to give centrist allies the information they need to craft common sense solutions, and provide those allies the support they need to turn those ideas into results.

In order to meet our challenges we need to put aside the partisan bickering that has gridlocked Washington and come together to find common sense solutions.

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passageways and tubes in their bodies. In 1983, the life expectancy for patients with Cystic Fibrosis was ten years. From 2000 to 2021, the FDA granted 107 Orphan Drug Designations for treating CF. Today, the life expectancy is 37 years.

Sickle cell provides another success story. Sickle cell disease is a group of red blood cell disorders that cause abnormal blood flow, leading to pain and other serious complications. Starting in 1979, the FDA began approaching various new treatments for sickle cell disease, raising the median age of survival from 28 to 43 years by 2017. In 2022, two new sickle cell treatments received orphan drug designations. These new treatments promise to help make sickle cell disease more manageable for 100,000 American patients. Most recently in 2023, FDA approved two gene therapies for sickle-cell therapies, including the first **CRISPR-based treatment**, a technology that research scientists use to selectively modify the DNA of living organisms.

Decreasing Incentives

While the Orphan Drug Act has helped bring many new treatments to the market, experts are concerned the legislation does not hold the same weight it once did. In 2017, the Tax Cut and Jobs Act reduced tax credits for rare disease research and development (R&D) from 50% to 25%. Companies working in the rare disease space often spend the majority of their revenue, if not all of it, on R&D. Changes in the orphan drug tax credit represent a significant challenge in their ability to operate from a cash flow perspective and ultimately their financial viability as a business. Additionally, the share of orphan drugs with exclusivity periods that extend beyond the drug's patent life continues to decline. Together, this means rare disease drug development is less profitable for pharmaceutical companies, resulting in fewer patients receiving potentially life-saving treatment.

The Inflation Reduction Act of 2022 (IRA) exempts orphan drugs indicated for only one rare disease from the Drug Negotiation Program. The cap of one rare disease was intended to prevent drugs that treat both rare and non-rare diseases from being exempt. However, the private sector believes the current policy disincentivizes pharmaceutical companies from pursuing additional rare disease indications of their orphan products. For example, Alnylam Pharmaceuticals Inc. cited the IRA's policy as the reason it halted research on a secondary rare disease indication. The potential secondary use would have resulted in the loss of their status as an exempted drug.

Underlying Challenges

Rare disease patients suffer difficult diagnostic journeys. The lack of awareness of rare diseases, combined with a shortage of specialists and access barriers, makes receiving a diagnosis for rare diseases a difficult process. The average time for an accurate diagnosis of a rare disease is 4.8 years but can reach up to 30 years in extreme cases. During this time, patients often see their conditions deteriorate with little knowledge about what is happening to them.

Recent technological advances such as gene panels, microarrays, and exome sequencing have helped diagnose patients with rare diseases. Some providers are using artificial intelligence (AI) methods to screen for specific conditions. For example, in 2017, ThinkGenetiuc Inc. introduced their AI tool "SymptomMatcher," a program that matches self-reported symptoms with those of rare diseases. Congress has also offered remedies to enhance the diagnostic process. The Newborn Screening Saves Lives Reauthorization Act would provide necessary resources to improve state programs that screen newborns for a complete panel of rare disorders and educate parents and providers on those disorders. Additionally, the Expanded Genetic Screening Act would allow Medicaid to cover the costs of noninvasive prenatal genetic screening, another tactic to identify rare diseases.

Research and development for pharmaceutical companies is a risky investment requiring immense startup capital. The percentage of drugs that actually reach the market is less than 2 percent, most of which fail during the "**valley of death**". The valley of death describes the period when research has begun, but the drug is not yet available commercially. During this time, pharmaceutical companies often require financial government support to sustain R&D efforts until the drug can turn a profit. A lesser-known second valley of death often occurs to companies having difficulty collecting reimbursements after the drug is on the market.

As a result of the 2017 Tax Cut and Jobs Acts, starting in the tax filing of 2022, the government "**amortized**" or spread the reimbursements of R&D expenses out over five years for domestic R&D investments and fifteen years for foreign R&D investments, as opposed to fully deducting on a yearly basis as has been the historical policy. The issue for R&D-intensive companies, such as pharmaceutical manufacturers and developers, can be twofold. Industry says the lack of cash flow from year to year inhibits how much one company can reinvest into R&D. Secondly, due to inflation, the money reimbursed to companies by the government five years after it was initially invested is worth less. R&D amortization has already resulted in the slashing of domestic R&D workforces of many rare disease companies and could drive innovation abroad where tax incentives for R&D are routinely higher - in some cases, twenty times as much.

The Center for Medicaid Services has recently applied a Coverage with Evidence Development (CED) policy to a new class of Alzheimer's drugs. This policy, initially instituted during the George W. Bush Administration, was intended for medical devices. Traditionally, any drug the FDA approved would be covered by CMS. The CED policy requires manufacturers to continue to test effectiveness and have patients enroll in clinical trials to be covered and reimbursed by CMS. This policy has not been used on any rare disease drugs, but the additional regulation from CMS could have a cooling effect on innovation in the industry.

Proposals for Improvement

Despite the success of the ODA, only 5% of the nearly 10,000 known rare diseases have an approved treatment. With plenty of room for progress, policymakers are considering options to bolster rare disease R&D. In 2012, Congress passed the Food and Drug Administration Safety and Innovation Act, which created the Rare Pediatric Disease Priority Review Voucher Program (RPD PRV). Under this program, sponsors that receive approval for a rare disease treatment also receive a voucher that entitles the company to receive a 6-month review instead of the FDA's standard 10-month review period. The RPD PRV has been impactful, resulting in dozens of therapies for children with rare conditions. With this program set to expire in 2024, Congress will have to evaluate its effectiveness. The program will continue to award vouchers to product applications with rare pediatric disease designations through 2026. Experts suggest extending or making the program permanent could help incentivize the production of rare disease treatments.

Over the past three years, Representative Josh Gottheimer (D-NJ) has repeatedly introduced "Cameron's Law". The legislation, named after Cameron Hyman, an eight-year-old struggling with Sanfilippo Syndrome, would restore the full value of the orphan drug tax credit. The bill would reverse the changes made in the 2017 Tax Cuts and Jobs Act that reduced tax credits for clinical testing from 50% to 25%. The legislation in the 118th Congress is co-sponsored by Representative Don Bacon (R-NE).

In 1992, Congress established the Accelerated Approval Pathway to expedite the approval and availability of drugs and biologics. The program uses **"surrogate" markers** at earlier points in the development process to facilitate earlier access to treatment. For rare diseases often the only traditional clinical trial endpoints can take years to manifest. Therefore, surrogate endpoints are a better way to approve certain rare disease treatments.

Congress is currently considering a bill that would eliminate the five-year amortization requirement for R&D expenditures. The legislation, titled the American Innovation and R&D Competitiveness Act, was introduced by Representatives Ron Estes (R-KS) and John Larson (D-CT) and a bipartisan group of 218 cosponsors. Estes and Larson argue that restoring the same-year R&D deduction is critical in ensuring the United States remains the global leader in R&D in healthcare and other industries.

Also this Congress, Representatives John Joyce (R-PA) and Wiley Nickel (D-NC) introduced the ORPHAN Cures Act. This legislation seeks to alter the provision in the Inflation Reduction Act that excludes rare-disease drugs with more than one approved indication from exempting the Drug Price Negotiations Program. The passing of this bill would allow rare-disease drugs with multiple indications to receive exemptions. Joyce and Nickel's bill has eight bipartisan cosponsors, a companion bill introduced in the Senate, and has received significant attention from stakeholders in the rare disease community.

Additionally, lawmakers have proposed initiatives to clarify the scope of the ODA. In 2021, the U.S. Court of Appeals for the 11th Circuit gave a decision on *Catalyst Pharms., Inc. v. Becerra,* which gave manufacturers exclusivity for drugs covering an entire condition, even if their treatment only has use for a certain subset of the patient population. As a result of this decision, the FDA was forced to withdraw marketing approval for a drug that provided treatment for Lambert-Eaton myasthenic syndrome, a rare autoimmune disease affecting 400 Americans. In 2022, Senators Tammy Baldwin (D-WI) and Bill Cassidy (R-LA) proposed the RARE Act, which would ensure the scope of the orphan drug exclusivity only applies to the same approved use or indication within a rare disease instead of covering the whole condition. This bill is supported by consumer representatives like the National Organization for Rare Diseases as a proposal that would make more treatments available for patients suffering from rare diseases.

The Path Forward

The United States is approaching a critical moment in rare disease research and development. New technologies are emerging for diagnostics and more treatment options are available for rare disease patients than ever before. However, this progress is challenged by the reduced orphan drug tax credit, R&D amortization, limiting approved indications, and the weakening of the intent of the Orphan Drug Act. Faced with these realities, policymakers will need to consider action to strengthen the United States' position at the forefront of rare disease R&D innovation. Involving industry, patient communities, and medical experts will be key to producing a productive policy that will ultimately lead to saving the lives of rare disease patients.

Links to Other Resources

- Johnson & Johnson - What is a Rare Disease
- NORD - Rare Disease Policy in Action
- NORD - The Orphan Drug Act Turns 40
- NORD - Understanding Rare Diseases
- National Library of Medicine - A Comprehensive Study of the Rare Dseases and Conditions Targeted by Orphan Drug Designations and Approvals Over the Forty Years of the Orphan Drug Act
- Summit Health - The Challenges of Treating Rare Diseases
- University of Chicago - The Orphan Drug Act at 35
- University of Southern California - Medicare's "Coverage with Evidence Development"