MARWOOD GROUP

Emerging Payor Countermeasures To Rare Disease Cost Impact

Executive Summary And Outline

The Orphan Drug Act (ODA) and subsequent legislation tackled the development shortfall for rare diseases. An unintended consequence has been a growing affordability crisis which has drawn attention from not only payors, but legislators as well. Herein, we address the current challenges faced by payors with respect to orphan drug affordability as well as emerging countermeasures to mitigate their impact.

I. The Growing Orphan Drug Affordability Challenge

Passage of the 1982 Orphan Drug Act (ODA) created financial incentives for the development of rare disease drugs. A host of additional development incentives (FIGURE 1) and relatively lower evidentiary bar have reduced manufacturer expenses, amortized them over a longer horizon (i.e., extended exclusivity) and driven rare disease drugs to over 50% of yearly FDA approvals. However, payors have seen spiraling cost impact (FIGURE 2).

II. Forces Exacerbating Orphan Drug Affordability Have Begun To Come Under Scrutiny

Outside of federal policy, a number of scientific and market forces have contributed to the growing share of FDA orphan drug approval and spend by payors. With the expansion of personalized medicine among biomarker-driven and genetically linked conditions, more products have qualified for orphan status over time, further catalyzing affordability concerns. Conversely, certain rare disease therapies have subsequently secured FDA approval for non-orphan indications. These “partial orphans” retain “orphan-level” pricing thus increasing burden on the healthcare system; neither manufacturer driven indication pricing nor payor-driven indication reimbursement currently exists to limit this practice.

Notably, the problem has reached mainstream attention with growing legislative movement toward closing loopholes that adversely impact payors. In the November 2021 House-passed Build Back Better package, the orphan drug tax credit would have only applied to those clinical testing expenses that were related to the first use or indication for rare disease condition. While never passed into law, it demonstrates legislator concern over what has been termed “salami-slicing’ of indications. More recently, in the Biden-signed Inflation Reduction Act, rather than indicate all orphan drugs excluded from negotiation, the text indicates that only certain orphan drugs are excluded – those that only target a single rare disease/orphan disease. Thus, drugs with multiple approved orphan designations are eligible for negotiation (barring other selection criteria).

III. Payors Face Limited Conventional Tools To Control Orphan Drug Spend

Medicare Part D and the ACA rules for individual and small-group products generally require coverage for prescription drugs that are the only product available in the class; as noted, many orphan drugs maintain natural monopolies. Consequently, price concessions are uncommon for orphan drugs, even when there are one or two competitors. This leaves utilization management restrictions on orphan products strictly to label or trial in an effort to encourage evidence-based prescribing. Further confounding payors are smaller, often unrandomized clinical studies with frequent use of surrogate endpoints; which are adequate to the FDA, yet frustrating to payors looking to utilize clinical trial evidence to frame coverage criteria. In oncology in particular, coverage requirements that align with compendia rules further restrict plans' ability to deny coverage.

However, partial orphans may prove financially attractive to generic manufacturers while providing some respite to payors. Through a practice known as "skinny labeling," generic manufacturers can produce a generic medication of a partial orphan drug with a label limited to the drug's non-orphan indication(s). The strategy relies on physicians prescribing off-label for the non-orphan indication and payors reimbursing for the off-label indication, even if unable to outright promote its off-label use.

Policies/Programs	Description
Extended Market Exclusivity	7 years of market exclusivity for approved orphan indications
Clinical Trial Tax Credits	*,**25% federal tax credit for expenditures incurred in conducting clinical research within the US
User Fee Waiver	Waiver of Prescription Drug User Fee Act (PDUFA) fees
Research Grants	Ability to compete for research grants from the Office of Orphan Products Development (OOPD) to support clinical studies for orphan drugs
340B Exemption	The Affordable Care Act (ACA) expanded eligibility for 340B discounts; for those additional covered entities, manufacturers are not required to provide 340B discounts for products with orphan designations
FDA Accelerated Approval	Allows for approval based on a surrogate endpoint
Rare Pediatric Disease Priority Review Voucher	A sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application
Negotiation Semi-Exclusion	***In the recently signed Inflation Reduction Act, rather than indicating all orphan drugs are excluded from negotiation, the text indicates that only certain orphan drugs are excluded – those who only target a single rare disease/orphan disease

Figure 1: Congress and the FDA have built on the ODA's original provisions to establish additional incentives and programs favoring orphan drug development. *Trump's tax cuts and Jobs Act, signed in 2017, slashed the orphan drug tax credit from the original 50% of the drug's clinical trial costs to 25%. **In the November 2021 House-passed Build Back Better package (not signed into law), the orphan drug tax credit would only apply to those clinical testing expenses that were related to the first use or indication for rare disease condition. *** A drug that has multiple approved orphan designations, under the 2023 Inflation Reduction Act is eligible for negotiation (barring all other selection requirements).

Drug	Company	List Price (USD)*
Zokinvy*	Eiger BioPharmaceuticals	$86,000
Myalept	Amryt Pharma	$72,159
Mavenclad	Merck KGaA	$60,371
Ravicti	Horizon Therapeutics	$57,998
Actimmune	Horizon Therapeutics	$55,310
Oxervate	Dompé	$48,498
Takhzyro	Takeda	$46,828
Juxtapid	Amryt Pharma	$46,502
Cinryze	Takeda	$45,465
Chenodal	Travere Therapeutics	$42,570
Gattex	Takeda	$41,664
H.P. Acthar	Mallinckrodt Pharmaceuticals	$39,864
Orladeyo	BioCryst Pharmaceuticals	$37,308
Tegsedi	Ionis Pharmaceuticals/Akcea Therapeutics	$35,638
Ayvakit	Blueprint Medicines	$33,568
Vitrakvi	Bayer	$32,800
Qinlock	Deciphera Pharmaceuticals	$32,000
Korlym	Corcept Therapeutics	$31,440
Cerdelga	Sanofi	$28,599
Idhifa	Bristol Myers Squibb	$28,246

*Source: GoodRx; *List prices for each medication calculate a 30-day prescription. Some drugs may not require continuous dosing.*

Figure 2: The 20 most expensive pharmacy drugs in the U.S. in 2021. Rare disease therapeutics average in the tens of thousands of dollars, with a growing number exceeding $1M per year.

IV. Emerging Payor Strategies To Manage Orphan Drug Spend

In balancing affordability and patient access to an increasing number of innovative, high-cost therapies, payors have applied traditional utilization management strategies, such as prior authorization requirements, step therapy, and quantity limits, to manage orphan drugs. Additional strategies to support ongoing affordability of these products, include innovative payment models and benefit design changes. Stop loss or reinsurance policies help manage extremely high, unanticipated costs that can be associated with some orphan treatments. However, cost-effectiveness of these benefit designs have been a lingering challenge, particularly in future context of curative therapy launches with $1M+ price tags.

Rare disease specific carve-out arrangements are an emerging strategy to protect fully insured plans and self–funded employer plans by contracting with a third party that assumes the risk for reimbursement, while also supporting coordination for patients and providers throughout the process. At the extreme, some employer-funded plans have resorted to stripping out high-cost orphan drugs entirely from their health benefit. The burden then falls on a growing number of patient assistance programs, a topic Marwood touched upon in its July 2022 whitepaper on HUB services.

Often working directly with the plan or through a PBM, the carve-out vendor assists in carving out specialty drugs from coverage while enabling support through patient assistance programs with links to manufacturers or charitable foundations. These alternate funding companies most likely utilizing proprietary software to find funding from manufacturers and foundations – often those most likely not to flag the arrangement.

There are currently ~20 players in this field which vary in the combination of features and their degree of approach. At their core, the process often looks as follows:

1. Specialty drugs are excluded from the plan's formulary, potentially following alignment with a carve-out vendor.
2. The vendor helps the patient appear as "uninsured" so they can apply for the manufacturer's patient assistance funds to cover the cost of the prescriptions.
3. The manufacturer pays the full cost of the prescription and the pharmacy services. Meanwhile, the plan sponsor incurs no costs for the specialty drug.
4. Either the payor passes on to the vendor a fraction of the cost of the drug, or the vendor retains a fraction of the value paid out by the patient assistance program, once they arbitrage the solution with a specialty pharmacy to supply the patient with the drug in the most cost-effective manner.
5. If a manufacturer's patient assistance program denies the patient, the carve-out vendor may seek to source products from pharmacies located outside the United States – a practice frowned upon by the FDA's BeSafeRx program.

V. Evaluating Third-Party Carve-out Vendors

Analysis of carve-out vendors requires a balanced view of patient, plan, manufacturer, and regulatory perspective:

Patient delays are possible. In these schemes, patients often face treatment delays due to the application process for patient assistance program funds. They may also be encouraged to use the product with a more favorable patient assistance program rather than the most clinically appropriate product.

Plan costs may increase. Plan sponsors incur higher administration costs, because the carve-out vendor must coordinate with the primary PBM that is administering the pharmacy benefit. The plan sponsor also faces higher plan costs due to higher fees or lower rebates and discounts from their PBM.

Manufacturer response is possible, particularly those managing patient assistance programs. Commercial payors are accessing need-based funds from charitable foundations that were established to help truly underinsured and uninsured patients.

Self-insured plans may in some circumstances face ERISA and IRS-related compliance issues. Manufacturers and agencies providing alternative funding may claim misrepresentation given alternative funding depends on recipients having no insurance. Plans may also be taking enormous safety risks, enabling carve-out vendors to source prescriptions from overseas pharmacies.

VI. Future Considerations

Orphan drug costs will continue to be a focus of payor, legislator and regulator concern. Target analysis in this environment requires an understanding of health plan/PBM strategies and emerging federal and state regulatory and legislative policies impacting both the rare disease and patient assistance program space. Notably, Marwood has experience conducting analysis on behalf of alternative drug sourcing programs. Marwood's services span federal and state regulatory and legislative considerations, payor/PBM dynamics from a Medicare, Medicaid and commercial perspective, strategic considerations of landscape and market sizing and compliance diligence.

About the Author

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