

# Orphan Drug Debate: A Cheat Sheet

**By Krishna R. Patel, PharmD** In some respects, the 1983 Orphan Drug Act is a success story. It changed the economics of developing drugs for rare diseases, so hundreds of treatments for diseases that affect relatively small numbers of people are now on the market. But high prices and allegations that some drug companies have twisted the law to their advantage have made it controversial. Here are some of the main points in the debate.

What payers say	What manufacturers say in defense	What patients, providers, and experts are saying
<b>ALMOST UNLIMITED PRICE TAGS</b>		
<p><b>Manufacturers charge premium prices for orphan drugs and payers have almost no choice but to pay for them.</b></p> <p>Median cost per patient in 2016 was <b>5.5x higher</b> for orphan drugs compared with non-orphan drugs (\$83,883 vs. \$15,239, respectively).</p> <p>Payers are <b>forced to cover orphan drugs</b> because they are the only options available for patients.</p> <p><b>Uncertain long-term benefit.</b> Orphan status has become synonymous with astronomical prices. It's hard for payers to rationalize spending so much money in the first year of treatment without knowing the long-term effectiveness of the orphan drugs.</p>	<p><b>Research and development for orphan drugs is long, costly, and risky.</b></p> <p><b>High prices are a reflection of the high cost of developing new orphan drugs.</b> Some companies focus on a therapeutic area for 20 or 30 years and never turn a profit. For example, it took 25 years for the development of an effective therapy for cystic fibrosis.</p> <p><b>Budget impact of orphan drugs is actually small.</b></p> <ul style="list-style-type: none"> <li>~1% of total U.S. health care spending. Payers are overstating the impact of high orphan drug prices; they cite high orphan drug prices as the reason for climbing premiums, copays, and coinsurance. However, rising medical costs have a much greater impact on rising costs.</li> </ul>	<p><b>Even though many patients and their families don't pay the full amount for orphan drugs, high prices make access doubtful.</b></p> <p><b>Insurance coverage and manufacturers' patient-assistance programs help to lower the out-of-pocket costs for patients.</b></p> <ul style="list-style-type: none"> <li>Patient-assistance programs are unavailable to patients covered by Medicare and Medicaid.</li> <li>Critics say manufacturers use patient-assistance programs to boost sales, burdening payers with the cost of covering high-priced drugs.</li> </ul> <p><b>Uncertainty of drug access can be a constant fear among patients and caregivers.</b></p> <ul style="list-style-type: none"> <li>Payer scrutiny of the potential budget impact of orphan drugs puts obstacles in the way of patient access. Cost sharing (copayments and coinsurance) and utilization management vary widely among insurance plans.</li> <li>There's always some uncertainty about the length and terms of patient-assistance programs.</li> </ul>
<b>RAPID GROWTH IN ORPHAN DRUG SALES</b>		
<p><b>Payers feel it is unsustainable to shoulder the rapid growth in orphan drug sales in the past four to five years. Currently, only 5% of rare diseases have treatment options; what happens if that was 95%?</b></p> <p>Worldwide annual sales from orphan drugs are projected to <b>grow twice as fast as the rate predicted for conventional drugs through 2020</b>, according to market watcher EvaluatePharma.</p> <p><b>Worldwide sales of orphan drugs are expected to almost double</b> between 2016 and 2022 to \$209 billion, accounting for 21.4% of total worldwide prescriptions sales, according to EvaluatePharma.</p> <p><b>Expenditures for oncology were the highest</b> among all major therapeutic areas. The next major therapeutic areas were infections, nononcology hematology, and metabolic disorders.</p>	<p><b>Rising concerns about the explosion of spending on orphan drugs are overblown.</b></p> <p>Reason for rapid growth in costs is due to an <b>increase in FDA approvals in recent years</b>—and that is a good thing. The number of orphan drug approvals increased from 16 in 2007 to 33 in 2013.</p> <p>U.S. orphan drug <b>expenditures will actually remain fairly stable</b> in proportion to total pharmaceutical expenditure (8.8% in 2014 to 9.5% in 2018), according to a study published in <i>Health Affairs</i>.</p> <p><b>True impact of orphan drugs has been overstated</b> in many studies that lump orphan drugs in with specialty medicines and precision medicines.</p>	<p><b>The Orphan Drug Act has saved lives and relieved suffering for many Americans with rare diseases.</b></p> <p>Despite the increasing number of orphan drug approvals in recent years, an unmet need exists even today, as only <b>5% of rare diseases have a treatment.</b></p> <p><b>Development of orphan drugs has added extraordinary value for patients.</b> Patient advocacy organizations and disease charities are the ones that push for initiation of research for orphan drugs. Note: Some say the advocacy groups and disease charities are too cozy with industry and are being used.</p>

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<b>GAMING THE SYSTEM</b>		
<p><b>Manufacturers are gaming the Orphan Drug Act of 1983 to receive millions of dollars in government incentives plus exclusivity rights.</b></p> <p>A loophole in the Orphan Drug Act allows manufacturers to receive <b>market exclusivity for older drugs</b> that are already available in markets outside the U.S.</p> <ul style="list-style-type: none"> <li>• Example: Emflaza, Marathon's drug for Duchenne muscular dystrophy, is priced at a premium even though patients had been buying it from other countries for only about \$1,500 a year. Furthermore, it is not seen as a scientific breakthrough as it is a corticosteroid that could be used more broadly.</li> </ul> <p><b>Partial orphan drugs</b> (drugs initially approved for the mass market that subsequently gain an indication for a rare disease) are rampant.</p> <ul style="list-style-type: none"> <li>• Examples include Crestor, Abilify, Herceptin, Botox, and Humira.</li> </ul> <p><b>Salami slicing</b> (artificially slicing the disease into smaller subgroups in order to gain orphan status and reap the accompanying benefits such as premium price tags, 50% tax credit on R&amp;D costs, and seven years of market exclusivity) is another way manufacturers are taking unfair advantage of the law.</p> <ul style="list-style-type: none"> <li>• Drugs indicated to treat <b>biomarker-defined subsets of common conditions</b>, especially cancer, comprised 16% of recently approved orphan drugs.</li> </ul> <p><b>Priority review vouchers have been sold</b> and been known to fetch up to \$350 million by manufacturers of orphan drugs in the open market.</p>	<p><b>Only a handful of approved orphan drugs were not in the "spirit" of the law and PhRMA castigates these offending manufacturers.</b></p> <p><b>Partial orphan drugs (older drugs subsequently repurposed for a rare disease) only accounted for 64 of the 316 (20%)</b> brand-name FDA-approved orphan drugs approved at the time of the analysis, according to a study by IMS Health researchers published in <i>Health Affairs</i>.</p> <p>After adjusting for sales specific to the rare disease indications only, <b>partial orphan drug expenditures were minimal</b>, representing 0.5% of total pharmaceutical expenditures in 2007 and 1.2% in 2013.</p> <p><b>Prices were similar</b> between <b>biomarker-defined drugs</b> and their non-biomarker-specific counterparts.</p> <p>Experts believe that <b>perhaps 3% of orphan drugs truly gamed the system</b>, by exploiting loopholes in the Orphan Drug Act.</p> <p><b>PhRMA, the drug industry's trade association, condemns</b> those manufacturers who game the system and has taken steps to sever ties with them.</p>	<p><b>The Orphan Drug Act of 1983 should be reassessed.</b></p> <p>Creators of the law, including patient advocacy groups as well as lawmakers, say that some manufacturers have undermined the spirit of a well-intended law.</p> <p>Expert suggestions for regulatory changes to maintain the spirit of the law:</p> <ul style="list-style-type: none"> <li>• When orphan drugs reach <b>blockbuster status</b> (\$1 billion in annual sales), <b>manufacturers should pay back some of the federal incentive money</b> through a back tax. Japan already does this.</li> <li>• In an effort to address partial orphan drugs, <b>those already on the market should be awarded weaker benefits</b> compared with new drugs.</li> <li>• The FDA should adopt increased scrutiny to avoid allocating benefits to manufacturers that engage in salami slicing.</li> </ul>

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