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Trends in Orphan Drug Spending And Out-of-Pocket Spending Among US Children, 2013–18

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Abstract

Among privately insured children, the proportion of inflation-adjusted total health care spending accounted for by orphan drugs increased from 4.0 percent to 6.6 percent between 2013 and 2018. This increase was largely driven by price growth. Mean annual out-of-pocket spending for orphan drugs rose from \$486 to \$866 and was higher for children than adults.

Pharmaceuticals designated “orphan drugs” are those with at least one Food and Drug Administration–approved indication to treat a rare disease under the Orphan Drug Act of 1983. The act defines rare diseases as those affecting fewer than two hundred thousand Americans.¹ Although most orphan drugs only have approved “orphan indications” to treat rare diseases, approximately one-fifth also have “nonorphan indications” to treat common diseases.²

Between 2009 and 2017, US orphan drug spending doubled to \$112 billion, or 24.9 percent of prescription drug spending in 2017.¹ This trend was driven by increasing orphan approvals and high orphan drug prices.^{1,2} However, it is unknown whether orphan drug spending has risen specifically among children, a population disproportionately affected by rare diseases.³

In this national study of privately insured children, mean annual out-of-pocket spending for orphan drugs increased from \$486 to \$866 (78.2 percent) (exhibit 1). In each year, mean annual out-of-pocket spending for orphan drugs was higher among children than among adults. In addition, the proportion of spending by children accounted for by orphan drugs rose from 4.0 percent to 6.6 percent between 2013 and 2018 (65.1 percent) (exhibit 2). Findings demonstrate that pediatric orphan drug spending is increasingly burdening payers and families and suggest that payers should better protect families against the prices of orphan drugs by improving benefit design.

This study contains three main analyses. First, we used national commercial claims to examine trends in orphan drug spending and out-of-pocket spending among children across all orphan drugs. Second, we stratified analyses according to whether orphan drugs were small-molecule drugs (low-molecular-weight drugs that are manufactured synthetically) or biologics (high-molecular-weight drugs derived from living organisms). Finally, to contextualize results in children, we also examined trends in orphan drug spending and out-of-pocket spending among adults.

Study Data And Methods

We analyzed the 2013–18 IBM MarketScan Commercial Database, which includes nonelderly enrollees across the US with insurance coverage from medium to large firms.⁴ Sample sizes were forty-four million in 2013 and forty-seven million in 2014, but fell to a range of twenty-seven to twenty-eight million in 2015–18 because of data contributor loss. However, demographic characteristics of children in our study were similar in all years, suggesting that changes in sample composition minimally affected results (online appendix).⁵ Because data were de-identified, the University of Michigan Institutional Review Board exempted this study from review.

For each year, we included children ages 0–17 years who were continuously enrolled with pharmacy benefit coverage. We excluded children with any capitated claims, which sometimes contain unreliable spending data.

We identified claims for 526 orphan drugs with at least one approved orphan indication by December 31, 2018, including claims for prescription fills and claims for drug administrations during visits (drugs are listed in the appendix).⁵ For each year, we calculated the proportion of children with at least one annual orphan drug claim (“pediatric orphan drug user”) and the annual number of these claims per user.

We calculated total spending by children in the sample by summing insurer reimbursement and out-of-pocket spending across all inpatient, outpatient, and pharmacy claims. We calculated the proportion of total spending accounted for by orphan drug claims and by orphan drug users and calculated spending per orphan drug claim. Among pediatric orphan drug users, we calculated mean and median annual out-of-pocket spending for orphan drugs and for all care (inpatient, outpatient, pharmacy).

To assess trends by drug class, we assessed use, spending, and out-of-pocket spending for orphan drugs that were biologics (identified on the basis of approval through biologic license applications) versus small-molecule drugs (appendix).⁵ Both are of policy interest. Although biologics have largely driven US prescription drug spending growth,⁶ several high-priced small-molecule orphan drugs were recently approved for rare pediatric diseases. These include nusinersen, a drug for spinal muscular atrophy priced at \$750,000 for the first year of treatment.⁷

To contextualize results, we repeated analyses among adults ages 18–64 meeting the same inclusion and exclusion criteria. We determined the ten orphan drugs accounting for the

most spending among children in 2018 and the five biologics and five small-molecule drugs accounting for the most spending each year.

To capture the full budgetary impact of orphan drug spending on payers and families, we included spending and out-of-pocket spending for orphan drugs across all uses. Spending and out-of-pocket spending were inflated to 2018 dollars using the Consumer Price Index for All Urban Consumers.⁸ To assess trends, we calculated percentage changes between 2013 and 2018, as well as compound annual growth rates.

A major strength of this study is its inclusion of pharmacy dispensing and drug administrations during health care visits for 526 orphan drugs, allowing comprehensive capture of orphan drug use and spending. Limitations include reliance on data from children with insurance coverage from medium to large firms.⁴ Results may not generalize to other privately insured children or to publicly insured children. In addition, we did not differentiate between spending for orphan versus nonorphan indications because of data limitations, including the lack of specific diagnosis codes for many rare diseases. Of US orphan drug spending in 2017, 38.6 percent was for orphan indications.¹ Among children, this proportion is likely higher, as the nonorphan indications of orphan drugs typically target common adult diseases.^{1,3}

Study Results

Sample Characteristics

The sample included 4.4–5.8 million children per year. Orphan drug users were slightly older than non-orphan-drug users, but were similar by gender and census region (exhibit 3).

Use

Between 2013 and 2018, the proportion of children who were orphan drug users changed minimally. The mean annual number of orphan drug claims per user increased 26.4 percent (exhibit 2).

Spending

The proportion of total spending by children accounted for by orphan drugs increased from 4.0 percent to 6.6 percent (a change of 65.1 percent based on unrounded values; compound annual growth rate, 10.5 percent). The proportion accounted for by orphan drug users increased from 11.1 percent to 14.5 percent (a change of 30.5 percent; compound annual growth rate, 5.5 percent). Spending per orphan drug claim increased from \$3,655 to \$5,467 (a change of 49.6 percent; compound annual growth rate, 8.4 percent) (exhibit 2).

Out-Of-Pocket Spending

Among pediatric orphan drug users, mean and median annual out-of-pocket spending for orphan drugs increased from \$486 to \$866 (a change of 78.4 percent) and from \$108 to \$210 (a change of 94.4 percent), respectively. The proportion for whom out-of-pocket spending for orphan drugs exceeded \$2,000 increased from 5.9 percent to 13.1 percent (a change of

122.0 percent). Mean annual overall out-of-pocket spending increased from \$2,331 to \$2,921 (a change of 25.3 percent) (exhibit 2).

Biologic Versus Small-Molecule Orphan Drugs

The proportion of children with at least one annual claim for biologic and for small-molecule orphan drugs changed minimally. The mean annual number of claims for biologic and small-molecule drugs among children who used these drugs increased modestly (exhibit 4). Spending per claim across all biologic orphan drugs grew just 16.0 percent (compound annual growth rate, 3.0 percent), going from \$5,792 to \$6,718, whereas spending per claim across all small-molecule orphan drugs grew 162.7 percent (compound annual growth rate, 21.3 percent), going from \$1,507 to \$3,959 (exhibit 4). The proportion of total spending by children accounted for by biologics rose from 3.2 percent to 4.4 percent, for a change of 39.6 percent. This compares with a change of 163.5 percent for small-molecule drugs, going from less than 1 percent of total spending by children to 2.2 percent of total spending by children. The proportion of orphan drug spending accounted for by biologics decreased from 79.4 percent to 67.2 percent (a change of –15.4 percent). Among children using biologics, mean annual out-of-pocket spending for biologics rose from \$719 to \$1,090 (a change of 51.7 percent).

Comparisons With Adults

The appendix includes a comparison of key outcomes by age group.⁵ In all years, spending per orphan drug claim and annual out-of-pocket spending on orphan drugs was higher in children than in adults (exhibit 1). In contrast to children, the proportion of orphan drug spending in adults accounted for by biologics rose from 63.9 percent to 68.8 percent (a change of 7.5 percent)

Top-selling orphan drugs among children

In 2018, the ten orphan drugs accounting for the most spending collectively accounted for 52.9 percent of pediatric orphan drug spending (exhibit 5). In each year, orphan drugs approved to treat short stature (somatropin) were at least two of the five top-selling biologics. In 2018, nusinersen and two cystic fibrosis drugs (ivacaftor and lumacaftor/ivacaftor) accounted for the three highest spending totals among small-molecule orphan drugs (appendix).⁵

Discussion

In this national study of privately insured US children, the proportion of spending accounted for by orphan drugs increased by two-thirds between 2013 and 2018, reaching one in fifteen dollars by 2018. The prevalence of pediatric orphan drug users changed minimally, and the annual number of orphan drug claims per user increased 26.4 percent. In contrast, spending per orphan drug claim increased 49.6 percent, suggesting that rising pediatric orphan drug spending was driven more by increasing price than use.

Price increases were particularly substantial for small-molecule orphan drugs (162.7 percent). Largely as a result, the proportion of total spending by children accounted for by

these drugs grew 163.5 percent. Prices and spending on biologics also grew, but at a slower rate. As a consequence, the proportion of pediatric orphan drug spending accounted for by biologics decreased 15.4 percent, in contrast to the 7.5 percent increase among adults.

The rapid growth in prices and spending for orphan drugs highlights the importance of assessing their comparative effectiveness and cost-effectiveness. Although such assessments were beyond the scope of our analysis, we note that in 2018, the three top-selling small-molecule orphan drugs among children in our study were lumacaftor/ivacaftor, ivacaftor, and nusinersen. All these drugs confer health benefits, but concerns regarding their cost-effectiveness have been raised.^{7,9}

Among pediatric orphan drug users, mean annual out-of-pocket spending for orphan drugs increased 78.4 percent, reaching \$866 by 2018. This spending varied widely. Median annual out-of-pocket spending increased 86.1 percent but only reached \$210 by 2018, indicating that many families remained well-protected from high orphan drug prices. However, the proportion of pediatric orphan drug users with annual out-of-pocket spending for orphan drugs exceeding \$2,000 increased from 5.9 percent to 13.1 percent, indicating that a rapidly rising share of families were poorly protected.

In each year, mean annual out-of-pocket spending for orphan drugs was higher among children than adults, potentially because spending per orphan drug claim was higher among children. This age-based difference suggests that families of pediatric orphan drug users may particularly benefit from efforts by private payers to improve orphan drug coverage.

Efforts to improve coverage should not solely be limited to orphan drugs. Despite rapid rises, out-of-pocket spending for orphan drugs still accounted for a minority of overall out-of-pocket spending among pediatric orphan drug users, the mean of which was \$2,921 in 2018. Private payers should minimize financial barriers to accessing all high-value medical care that pediatric orphan drug users may require.

Conclusion

Orphan drugs account for a rapidly growing share of health care spending among privately insured children, mostly because of rising prices. To mitigate access barriers, private payers should reduce exposure to these prices by improving benefit design.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Notes

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Exhibit 1.

Mean annual out-of-pocket spending for orphan drugs among pediatric and adult users of orphan drugs, 2013–18

Exhibit 2:

Use, spending, and out-of-pocket spending for orphan drugs among children

Outcome	Year					Change (%) ^a		CAGR (%) ^b
	2013	2014	2015	2016	2017	2018		
Use								
Percent of children with at least one orphan drug claim (orphan drug users)	0.56	0.63	0.75	0.62	0.60	0.58	3.0	0.6
Annual number of orphan drug claims per user	5.4	5.2	5.4	6.1	6.6	6.9	26.4	4.8
Spending								
Percent of total health care spending on orphan drugs	4.0	4.4	5.2	5.6	6.5	6.6	65.1	10.5
Spending per orphan drug claim	\$3,655	\$3,817	\$3,854	\$4,711	\$5,259	\$5,467	49.6	8.4
Percent of total health care spending by orphan drug users	11.1	11.9	13.5	13.7	14.3	14.5	30.5	5.5
Annual out-of-pocket spending on orphan drugs among orphan drug users								
Mean	\$486	\$495	\$565	\$715	\$779	\$866	78.4	12.3
Median	\$108	\$95	\$154	\$162	\$202	\$210	94.4	14.2
25th–75th percentile	\$27–\$46	\$27–\$431	\$40–\$523	\$32–\$710	\$31–\$875	\$25–\$894	N/A	N/A
Percent of users with out-of-pocket spending for orphan drugs of at least \$2,000	5.9	6.4	7.6	11.0	12.1	13.1	122.0	17.3
Annual overall out-of-pocket spending among orphan drug users								
Mean	\$2,331	\$2,379	\$2,489	\$2,696	\$2,776	\$2,921	25.3	4.6
Median	\$1,571	\$1,658	\$1,818	\$2,100	\$2,224	\$2,320	47.7	8.1
25th–75th percentile	\$614–\$3,276	\$695–\$3,276	\$765–\$3,516	\$866–\$3,947	\$923–\$4,080	\$997–\$4,250	N/A	N/A
Percent of users with out-of-pocket spending	11.9	11.9	12.7	15.4	16.2	18.1	52.1	8.7

SOURCE: Authors' analysis of 2013–18 IBM MarketScan Commercial Database. NOTES: CAGR is compound annual growth rate. N/A is not applicable.

^aPercentage change between 2013 and 2018, based on unrounded values.^bCAGR = [(2018 value/2013 value)^{1/5} – 1].

Exhibit 3:

Characteristics of pediatric orphan drug users and non-orphan-drug users

	Orphan drug users	Non-orphan-drug users
Number of person-years ^a	176,694	28,242,820
Age		
Mean age (years)	11.0	9.2
0–5 years (%)	15.4	27.6
6–11 years (%)	32.1	33.7
12–17 years (%)	52.5	38.7
Gender		
Female (%)	46.9	48.9
Census region (%)		
Northeast	20.3	17.3
Midwest	21.8	22.3
South	41.1	41.2
West	15.3	17.7
Unknown	1.4	1.6

SOURCE Authors' analysis of 2013–18 IBM MarketScan Commercial Database.

^aThe sample included 4.4–5.8 million children per year, resulting in 28.4 million person-years of data from 11.9 million unique children. Percentages in the table were calculated at the level of person-years, not unique children.

Exhibit 4: Use, spending, and out-of-pocket spending on biologic and small-molecule orphan drugs among children

Outcome	Year							Change (%) ^a	CAGR (%) ^b
	2013	2014	2015	2016	2017	2018			
Use									
Percent with at least one claim for biologics	0.26	0.27	0.28	0.31	0.32	0.33	28.6	5.2	
Percent with at least one claim for small-molecule drugs	0.35	0.40	0.52	0.36	0.34	0.31	-12.6	-2.7	
Annual number of biologic claims per child with at least one biologic claim	6.0	6.0	6.2	6.1	6.5	6.6	10.4	2.0	
Annual number of small-molecule drug claims per child with at least one claim for small-molecule drugs	4.3	4.1	4.4	5.2	5.6	5.9	35.4	6.3	
Spending									
Percent of total spending on biologics	3.2	3.4	3.7	4.1	4.5	4.4	39.6	6.9	
Percent of total spending on small-molecule drugs	0.8	1.0	1.4	1.5	2.0	2.2	163.5	21.4	
Percent of orphan drug spending on biologics	79.4	77.5	72.0	72.6	69.8	67.2	-15.4	-3.3	
Spending per claim for biologics	\$5,792	\$6,024	\$6,469	\$6,888	\$7,024	\$6,718	16.0	3.0	
Spending per claim for small-molecule drugs	\$1,507	\$1,686	\$1,891	\$2,561	\$3,330	\$3,959	162.7	21.3	
Out-of-pocket spending									
Mean annual out-of-pocket spending on biologics among biologic orphan drug users	\$719	\$784	\$857	\$952	\$1,021	\$1,090	51.7	8.7	
Mean annual out-of-pocket spending on small-molecule drugs among small-molecule orphan drug users	\$257	\$251	\$355	\$410	\$420	\$471	83.6	12.9	

SOURCE Authors' analysis of 2013–18 IBM MarketScan Commercial Database. NOTES In this table, “biologics” refers to orphan drugs that are biologics; “small-molecule drugs” refers to orphan drugs that are small-molecule drugs. CAGR is compound annual growth rate.

^aPercentage change between 2013 and 2018, based on unrounded values.

^bCompound annual growth rate = $[(2018 \text{ value}/2013 \text{ value})^{1/5} - 1]$.

Exhibit 5:

Orphan drugs accounting for the ten highest spending totals among children in 2018

Generic name	Brand name	Percent of orphan drug spending in 2018	Disease targeted by orphan indication
Somatropin	Norditropin	10.6	Growth hormone deficiency
Somatropin	Humatrope	10.5	Growth hormone deficiency
Infliximab	Remicade	8.0	Crohn's disease, ulcerative colitis
Adalimumab	Humira	6.7	Juvenile idiopathic arthritis, hidradenitis suppurativa ^a , panuveitis ^b
Lumacaftor/ivacaftor	Orkambi	4.1	Cystic fibrosis
Nusinersen	Spinraza	3.5	Spinal muscular atrophy
Ivacaftor	Kalydeco	2.5	Cystic fibrosis
Dornase alfa	Pulmozyme	2.4	Cystic fibrosis
Somatropin	Genotropin	2.4	Growth hormone deficiency
Clobazam	Onfi	2.2	Lennox-Gastaut syndrome ^c

SOURCE Authors' analysis of 2013–18 IBM MarketScan Commercial Database. NOTES

^aDisorder characterized by recurrent boils.^bInflammatory eye disorder.^cSeizure disorder.