MEDICAID EVIDENCE REVIEW AND COST INITIATIVE BRIEF

Voxelotor (Oxbryta) for Sickle Cell Disease

OVERVIEW

In 2019, the US Food and Drug Administration (FDA) gave voxelotor accelerated approval as a treatment for sickle cell disease (SCD).[1,2] In September 2024, voxelotor's manufacturer voluntarily withdrew the drug from the market citing safety concerns.[3] SCD is a serious, inherited, painful, multisystem, and chronic blood disorder that affects around 100,000 individuals in the US, with more than half of those individuals (52,524) enrolled in Medicaid, 87% of whom identify as non-Hispanic Black.[4-6] People with SCD use more health care than those without SCD, and they may also face issues when accessing quality care, including lower rates of preventive care and difficulty obtaining adequate pain treatment.[7,8]

Generally, a comprehensive care model approach is needed to support individuals with SCD. This may include drug therapy to reduce complications (i.e., hydroxyurea, L-glutamine oral powder, crizanlizumab, voxelotor), hematopoietic stem cell transplantation, gene therapy, and medication to treat chronic pain.[5,9,10] Because more than half of the US population with SCD is insured by Medicaid, and because Medicaid is required to cover

MERCI Aims

The Medicaid Evidence and Review of Cost Initiative (MERCI) describes policy considerations for drugs approved by the US Food and Drug Administration (FDA) through the accelerated approval pathway. This brief provides information on:

- The estimated prevalence of target diagnoses (the accelerated approval drug's indication[s]) among Medicaid members;
- The clinical trial population used to support FDA approval, and how similar it is to Medicaid members overall; and
- Projected drug costs for state Medicaid programs, including a breakdown of state and federal funds using the Federal Medical Assistance Percentage (FMAP).

MERCI analyses include national and state-level data where available to inform budget and policy decisions by state and federal policymakers.

FDA-approved drugs for which the drug manufacturer has signed a rebate agreement with the US Department of Health and Human Services,[11] any treatments for SCD have the potential to incur significant public expenditures by state and federal governments.

Voxelotor was given accelerated approval based on a surrogate outcome of increases in hemoglobin.[1,2] In the FDA-required postmarketing trials, the manufacturer reported a higher rate of vaso-occlusive crisis and more deaths in the group receiving voxelotor as compared with those receiving placebo.[3] The uptake rates of voxelotor in Medicaid are estimated at less than 10%, yet according to our analysis, Medicaid spent more than $100 million on voxelotor for SCD treatment in 2020 and 2021 combined. This creates a precarious situation for individuals with SCD, for their health care providers, and for Medicaid officials who want to ensure provision of effective care for their members while stewarding scarce public dollars.

What Is Sickle Cell Disease?

A serious, inherited, multisystem, and chronic blood disorder, SCD is caused by a genetic mutation in the hemoglobin (Hb) beta chain, the red blood cell protein that binds to and transports oxygen throughout the body.[5] Because of this mutation, red blood cells (RBCs) change from a disc shape to a sickle shape, leading to their premature destruction (i.e., hemolytic anemia) and obstructing blood flow (i.e., vaso-occlusive crisis [VOC]) because the mutated cells are harder and stickier than normal RBCs.[5,12] The RBC sickling and obstructed blood flow leads to a wide

Sources. Information sourced from IPD Analytics and the FDA websites, unless otherwise referenced. Estimates of costs to Medicaid are based on our analysis presented in the section about historica Medicaid spending on voxelotor.
Abbreviations. CDC: Centers for Disease Control and Prevention; FDA: US Food and Drug Administration.

range of acute and chronic health complications affecting nearly every organ in the body; these complications may include chronic pain, serious lung problems, stroke, and vision loss, among others.[5,13] The extensive complications of SCD result in significant morbidity and mortality.[4,5,13] Life expectancy at birth is around 53 years for people with SCD,[14] more than 20 years shorter than life expectancy in the general US population.[15] The life expectancy gap may be even higher for people with severe SCD.[7]

The Centers for Disease Control and Prevention (CDC) estimates that SCD affects around 100,000 people in the US, with the disease most prominent in Black or African American populations.[4] Around 1 in 365 Black or African American babies are born with SCD.[16] The rates of SCD vary by state, with higher rates in the southeastern US, mirroring racial demographics of the US.[6,8]

In addition, roughly half of the SCD population in the US are Medicaid members.[6,7,14] The number of physicians (both specialists and primary care providers) trained and willing to treat SCD patients insured by Medicaid, especially adult patients, is limited.[7,8] For example, significantly fewer Medicaid members with SCD had visited a hematologist (a specialist in blood disorders) during the past year compared with individuals insured privately.[17]

How Is Sickle Cell Disease Managed?

Most of the available treatment options for SCD are for management of disease symptoms and complications, including VOCs and pain. Interventions approved by the FDA for SCD include L-glutamine oral powder, crizanlizumab, hydroxyurea, and voxelotor.[18] People with SCD may also receive blood transfusions to treat and prevent SCD related complications.[18]

There are also a few SCD treatment options which are potentially curative. One such treatment is allogeneic hematopoietic stem cell transplantation (HSCT; also known as a bone marrow transplant).[9] Although HSCT has a high success rate, access is limited because of donor availability, socio-cultural and economic barriers, and the risk for transplant-related complications and mortality.[9] In December 2023, the FDA also approved 2 gene therapies for SCD; both therapies are made from the person's own blood stem cells, which are harvested, modified, and transplanted back as a one-time, single-dose infusion.[10] These also may provide long-lasting or permanent results.[10]

How Much Does Sickle Cell Disease Cost to Treat?

Based on 2009 data from Medicaid, the annual cost to treat people with SCD in the US was estimated at more than $1.1 billion.[8,19] In 2009 dollars, the total lifetime health care cost for a person with SCD was approximately $9 million, with estimated annual costs ranging from $35,500 to $112,000 for children and averaging $231,000 for adults.[8,20] High rates of hospitalization, emergency department visits, and hospital readmissions may all contribute to the high treatment costs for SCD.[8]

DRUG INFORMATION

In 2019, voxelotor (branded as Oxbryta) was approved for the treatment of SCD in adults and children aged 12 and older through the FDA's accelerated approval pathway.[1,2] The approval was based on increases in Hb as a surrogate biomarker endpoint.[1,2] In 2021, the indication for voxelotor was expanded to children aged 4 up to 11 years, again through the accelerated approval process.[1,21] The drug manufacturer made voxelotor available through a specialty pharmacy partner network.[22] The mechanism of action involves the binding of voxelotor to Hb.[1]

DRUG SUMMARY

DRUG CLASS
Hemoglobin S polymerization inhibitor

MANUFACTURER
Global Blood Therapeutics Inc., Pfizer

PRICE PER PATIENT
$147,389 per year

PATHWAY Accelerated approval

DATE November 2019

PRESCRIBING LABEL
https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/213137s012,216157s003lbl.pdf

For the treatment of sickle cell disease in adults and pediatric patients 4 years of age and older

ROUTE Oral

FORMULATIONS
300 mg tablet
500 mg tablet
300 mg tablet for oral suspension

INFORMATION
Adults and pediatric patients 12 years and older: 1,500 mg orally once daily
Pediatric patients 4 to less than 12 years: based on body weight

BOXED WARNINGS None

PRECAUTIONS
Hypersensitivity reactions: Observe for signs and symptoms and manage promply.
Laboratory test interference: Perform quantification of hemoglobin species when patient is not receiving voxelotor.

ADVERSE REACTIONS
In adults: headache, diarrhea, abdominal pain, nausea, rash, and pyrexia (fever)
In children: pyrexia, vomiting, rash, abdominal pain, diarrhea, and headache

Note. Information reflects that of the most recent prescribing label and not that of the original accelerated approval.
Sources. IPD Analytics and the US Food and Drug Administration (FDA).

FINDINGS

What Evidence Was Used by the FDA to Approve Voxelotor?

Exhibit 1 provides a summary of the studies used to approve voxelotor through the accelerated pathway.

Why Did the FDA Grant Accelerated Approval?

The FDA considered results from the HOPE study, in which 182 people were randomized to receive 1 or 2 doses of voxelotor (900 mg or 1,500 mg) and 92 people were randomized to receive placebo.[1] When compared with placebo, significantly more people (51.1% vs. 6.5%) who received

EXHIBIT 1

Summary characteristics of the studies used to support efficacy of voxelotor

	HOPE[23,24]	HOPE Kids 1[25,26]
Official title	A phase 3, double-blind, randomized, placebo-controlled, multicenter study of voxelotor administered orally to patients with SCD	A phase 2a, open-label, single and multiple dose study to evaluate the pharmacokinetics, safety, tolerability, and treatment effect of GBT440 in pediatric participants with SCD
ClinicalTrials.gov ID	NCT03036813	NCT02850406
Clinical trial phase	Phase 3	Phase 2a
Study population description	274 adults and children (aged 12 to 65 years) with SCD	45 children (aged 4 to 11 years) with SCD
Blood hemoglobin (Hb) level requirements	To be eligible, participants had to have a blood Hb level of 5.5 to 10.5 g/dL	To be eligible, participants had to have a blood Hb level ≤ 10.5 g/dL
Vaso-occlusive crisis (VOC) requirements	To be eligible, participants needed to have had 1 to 10 VOCs within 12 months prior to the study	No eligibility requirement regarding VOCs prior to the study
Hydroxyurea requirements	Participants who were already taking hydroxyurea before the trial were eligible if their prescribed dosage of hydroxyurea was stable for 3 months prior to the study	Participants who were already taking hydroxyurea before the trial were eligible if their prescribed dosage of hydroxyurea was stable for 3 months prior to the study
Intervention	Voxelotor, 900 mg orally once per day Voxelotor, 1,500 mg orally once per day	Voxelotor, 600 mg, 900 mg, or 1,500 mg orally once per day, based on participant weight
Control	Placebo, orally once per day	No comparator group
Primary outcome used for accelerated approval	Increase in Hb of 1.0 g/dL	Increase in Hb of 1.0 g/dL
Trial funding	Global Blood Therapeutics, Inc. (Pfizer, Inc.)	Global Blood Therapeutics, Inc. (Pfizer, Inc.)

Sources. This information is taken from the trial publications and ClinicalTrials.gov trial registry records and may vary to that reported in the prescribing label.
Abbreviations. Hb: hemoglobin; SCD: sickle cell disease; VOC: vaso-occlusive crisis.

voxelotor at the higher dose (1,500 mg) had an increase from baseline in Hb of at least 1.0 g/dL at 24 weeks.[1]

The FDA also considered results from the HOPE Kids 1 study that evaluated the effectiveness of voxelotor in 45 children.[1] Overall, 36% of children who received at least 1 dose of voxelotor had an increase in Hb of 1.0 g/dL or greater at 24 weeks from baseline; there was no comparator group.[1]

Voxelotor does not have any boxed warnings; however, the current prescribing label highlights the most common adverse reactions for adults as headache, diarrhea, abdominal pain, nausea, rash, and fever; and for children (aged 4 to 11) as fever, vomiting, rash, abdominal pain, diarrhea, and headache.[1]

What Studies Were Requested to Convert Voxelotor to Full Approval?

As part of the accelerated approvals in 2019 and 2021, the FDA requested complete follow-up data from the HOPE RCT and complete study data from another ongoing RCT in children (HOPE Kids 2; NCT04218084).[27,28] For this brief, we requested further information from the drug's manufacturer on any ongoing studies intended to support conversion to full approval, but received no response at the time of writing.

The request for complete follow-up data from the HOPE trial is no longer active in the FDA's database of accelerated approvals[27]; however, at the time of writing this brief, voxelotor has been voluntarily withdrawn by the manufacturer after

EXHIBIT 2

Summary characteristics of the studies requested to support full approval

	PMR 3746-2[28,24]	PMR 3746-1 and PMR 4190-1[27,29]
ClinicalTrials.gov ID	NCT03036813[a]	NCT04218084
Study name	HOPE	HOPE Kids 2
Study population description	449 adolescents and adults (aged 12 to 65 years) with SCD	236 children (aged 2 to 14 years) with SCD
Primary outcome	Increase in Hb of 1.0 g/dL from baseline at week 24	Change in TAMMV arterial cerebral blood flow, as measured by transcranial doppler, at 24 weeks
Outcomes requested by the FDA	Complete follow-up data, with an updated safety and efficacy analysis	Change in TAMMV arterial cerebral blood flow, as measured by transcranial doppler, at 24, 48, and 96 weeks
Estimated date of final report submission at the time of accelerated approval	September 2020	September 2026, with an interim report in July 2025
Status of requested study	Completed; published in April 2021[30]	Active, not recruiting
Primary completion date	October 2019 (actual)	August 2023 (actual)

Note. [a] Initial findings used to support accelerated approval.
Sources. This information is taken from the trial publications and ClinicalTrials.gov trial registry records and may vary from that reported in the accelerated approval record.
Abbreviations. FDA: US Food and Drug Administration; PMR: postmarketing requirement; SCD: sickle cell disease; TAMMV: time averaged maximum of mean velocity.

reporting a higher rate of vaso-occlusive crisis and more deaths in the group receiving voxelotor as compared with those receiving placebo.[3]

How Common Is Sickle Cell Disease Among Medicaid Members?

Voxelotor is approved for the treatment of SCD in patients 4 years of age and older.[1] Of the 73,930,771 people aged 4 to 64 enrolled in the Medicaid cohort in 2021 (excluding the dually enrolled members), we identified 45,625 (or 6.2 per 10,000 members) as having SCD.

SCD was most common among Black Medicaid members (89.5% vs. 10% among other races and ethnicities); female members (55% vs. 45%); and members younger than 35 (81% vs. 19% among those aged 35 to 64; Exhibit 3).

The prevalence of SCD among state Medicaid populations varied considerably among the states with available data, from fewer than 0.8 cases per 10,000 members in Oregon, to 20.4 cases per 10,000 members in Mississippi. SCD was most common in Southeastern states, with Delaware, Florida, Georgia, Louisiana, Maryland, Mississippi, and South Carolina each experiencing SCD rates above 10 cases per 10,000 members (Exhibit 4).

EXHIBIT 3

Characteristics of Medicaid members aged 4 to 64 years with and without SCD, 2021

	with SCD[a]	%[b]	without SCD[a]	%[b]
Total members	*45,625*	-	*73,885,146*	-
Age, in years				
4 to 11	11,249	24.7	16,408,959	22.2
12 to 17	8,177	17.9	12,117,918	16.4
18 to 34	16,750	36.7	22,914,871	31.0
35 to 64	8,863	19.4	22,108,274	29.9
Sex				
Female	24,548	55.1	40,108,761	54.7
Male	20,019	44.9	33,257,735	45.3
Race and ethnicity				
American Indian/Alaska Native, non-Hispanic	78	< 1	790,969	1.5
Asian, non-Hispanic	170	< 1	2,202,505	4.3
Black, non-Hispanic	24,865	89.5	10,666,087	20.7
Hawaiian/Pacific Islander	21	< 1	249,447	< 1
Hispanic	1,575	5.7	15,436,985	29.9
White, non-Hispanic	857	3.1	21,603,062	41.9
Multiracial, non-Hispanic	199	< 1	474,192	< 1
Other race or ethnicity	29	< 1	174,688	< 1

Notes. [a] Excluding dually eligible members; the lower age limit is based on the drug indication and the upper age limit is based on Medicare eligibility. [b] Percentage of members with nonmissing data on demographic characteristics. 44,567 (97.7%) of the members with the drug indication and 73,366,496 (99.3%) of the members without drug indication had nonmissing information on sex. 27,794 (60.9%) of the members with the drug indication and 51,597,935 (69.8%) of the members without drug indication had nonmissing race/ethnicity data. For more detail see Appendix C.

DATA METHODS SUMMARY

Researchers at the Center for Evidence-based Policy (Center) used Centers for Medicare & Medicaid Services (CMS) Transformed Medicaid Statistical Information System (T-MSIS) and associated T-MSIS analytic files (TAF) to identify Medicaid members with the drug indication (beneficiaries aged 4 to 64 years with at least 1 inpatient or at least 2 outpatient claims with a SCD diagnosis [ICD-10 D57, except D57.3 sickle cell trait]) and their demographic characteristics, health states, and health care service use using applicable ICD-10 (International Classification of Diseases, 10th Edition) diagnosis codes, procedure codes, and NDCs (National Drug Codes).

The initial population for analysis included all Medicaid members aged 64 years or younger, with no months of dual enrollment in the years 2019, 2020, and 2021. Using these criteria, Utah and Alabama were excluded as they do not report dual-enrollment status using this method. Other state-based analysis exclusions were determined based on recommendations from the CMS Data Quality Atlas, which reports state-specific data availability and completeness; we excluded data elements identified as "unusable" and made exclusion decisions on a case-by-case basis for data elements identified as "unusable".

Drug indication cohorts for analysis were anchored in 2021, with a 3-year lookback period employed to ensure comprehensive Medicaid member identification for cohort inclusion. To make comparisons with the Medicaid population at large, we used a 3-to-1 exact matching method based on state, age (in years), sex, and race/ethnicity. Our cost model considered annual voxelotor costs estimated using inputs of drug indication prevalence, drug uptake, and adherence observed in TAF, as well as reported drug acquisition costs and statutorily required rebates. Refer to Appendix A for additional detail on how we conducted this study.

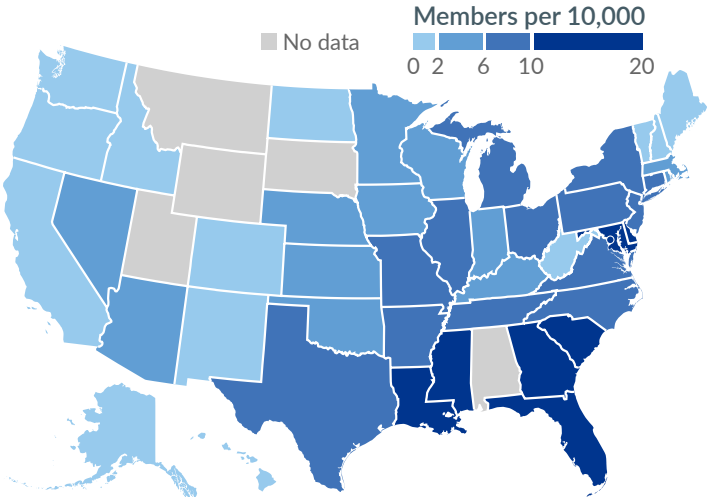
Still, even in states with higher SCD rates, those with the disease accounted for less than 1% of state's total Medicaid members. For example, we identified 3,182 members with SCD in Georgia, accounting for just 0.2% of the state's 1.9 million Medicaid members aged 4 to 64 years (see Appendix B for state prevalence estimates and Appendix C for characteristics of members with SCD in each state).

How Do Medicaid Members with Sickle Cell Disease Compare With the Voxelotor Trial Populations?

There are 2 primary studies that supported accelerated approval for voxelotor. The HOPE 1 Kids trial focused on youth aged 4 to 11 years,[25] and the HOPE trial enrolled people aged 12 and older.[23] The demographic characteristics of the patients included in the HOPE trial were similar to

EXHIBIT 4

Sickle cell disease prevalence among Medicaid members aged 4 to 64 years, per 10,000 members, by state, 2021



Note. [a] Data not available for Alabama and Utah. Data suppressed for Montana, South Dakota, and Wyoming (N < 11).

those observed in our analysis of Medicaid data. For example, the HOPE cohort was 58% female compared with 55% in our study.[23] Our Medicaid cohort was 89.5% Black, 5.7% Hispanic, and 3.7% White, with other race and ethnicity categories represented at less than 1%; the HOPE cohort was 67% Black, 22% Arab/Middle Eastern, and 9% White, with other race and ethnicity categories represented at less than 5%.[23] The HOPE and HOPE 1 Kids trials did not report on participant Medicaid eligibility or income level; it is unknown how well Medicaid members are represented in those trials.[23,25]

Medicaid members with SCD are sicker and use more health care than members without SCD. To contextualize the potential spending impact of SCD for state Medicaid programs, we examined the prevalence of select comorbidities, as well as hospital and emergency department use among Medicaid members aged 4 to 64 years, with and without SCD.

Our analysis showed that individuals with SCD were generally 2 to 4 times more likely to have comorbid diagnoses across all major body systems, compared with members without SCD; notably, SCD patients were 9 times more likely to experience stroke than members without SCD. See Appendix D for a table summarizing the prevalence of affected body systems and conditions in Medicaid members with and without SCD.

Members with SCD also had substantially higher hospital and emergency use than their matched comparisons. (See Appendix D for health care service use by Medicaid members with and without SCD.) Specifically, 44% of Medicaid members with SCD experienced at least 1 hospitalization in 2021, compared with 6% of members without SCD. Members with SCD also experienced more total inpatient days (706 vs. 45 per 1,000 members), were more likely to experience hospital stays lasting at least 5 days (22.5% vs. 2%), and had higher emergency room use across multiple measures. These patterns generally held across states; refer to Appendix D for summaries of selected health care service use measures for each state.

How Common Is Voxelotor Use Among Medicaid Members With Sickle Cell Disease?

Voxelotor became available in November 2019. From then through 2021, 6.6% of Medicaid members aged 12 to 64 years with SCD had at least 1 pharmacy claim for voxelotor (note: voxelotor was approved for individuals aged 12 and older in November 2019, and later approved for children aged 4 to 11 years in December 2021). In 2021 alone, voxelotor uptake among Medicaid members aged 12 to 64 was 5.4%. In comparison, voxelotor uptake was 4.6% in 2021 among individuals with SCD covered by private insurance.[31] Nationally, voxelotor use in Medicaid was consistent among eligible SCD patients across age, sex, and race and ethnicities (Exhibit 5), though uptake of the drug varied by state. Of the 31 states with enough eligible patients and pharmacy claims for analysis, voxelotor use varied more than five-fold, with just 2.8% of eligible SCD members receiving the drug in Arkansas and Wisconsin, and more than 15% of those eligible in Arizona and Rhode Island receiving the drug (see Appendix E, Table E1 for state information on voxelotor uptake).

Among eligible members with SCD prescribed voxelotor, only about one-third used the medication consistently over time. We considered medication adherence among eligible members prescribed voxelotor in 2021 using the Medication Possession Ratio (MPR), a member-level metric describing the ratio of total days supplied to days in the measurement year. Each member's measurement year began at the date of their first medication fill and ended on the last day of 2021. A member was considered "adherent" if their individual MPR was at least 0.8, meaning they possessed their medication on at least 80% of the days in their measurement year. In 2021, 34.6% of eligible members prescribed voxelotor demonstrated adherence at this level; the mean

EXHIBIT 5

Voxelotor uptake among eligible Medicaid members with sickle cell disease, 2019 to 2021

	All eligible members[a]	Using voxelotor	Not using voxelotor	% uptake
Total members	*34,046*	*2,261*	*31,785*	*6.6*
Age, in years				
4 to 11	*0*[a]	*0*[a]	11,579	*0*[a]
12 to 17	8,433	593	7,840	7.0
18 to 34	16,750	1,115	15,635	6.7
35 to 64	8,863	553	8,310	6.2
Sex				
Female	19,069	1,263	17,806	6.6
Male	14,250	967	13,283	6.8
Race and ethnicity				
Black, non-Hispanic	18,549	1,097	17,452	5.9
Hispanic	1,145	82	1,063	7.2
White, non-Hispanic	640	37	603	5.8
Other race or ethnicity	361	12	349	3.3

Note. [a] Medicaid members aged 4 to 11 years were not eligible for voxelotor treatment for most of the period 2019 through 2021; voxelotor was approved for these individuals on December 17, 2021.

MPR for the cohort was 0.61 (61% of the days in the measurement year).

It is unknown from the MPR why a patient might stop taking the drug; for example, they may have experienced adverse effects. However, it is known that the MPR is susceptible to member Medicaid enrollment status, which will affect the proportion of fills that can be identified in claims data. The mean MPR and the adherence rate was higher among members who were fully enrolled compared with those who were not (see Appendix E, Table E2 for more detail).

What Was the Impact of Voxelotor on Medicaid Spending in 2020 to 2021?

We estimated that total Medicaid spending on voxelotor was $115.2 million nationally from when it first became available for use in November 2019 through 2021, with $82.9 million of this cost coming from federal funds and the remaining $32.2 million coming from state funds. This estimate is based on converting the total number of days-supply in voxelotor claims into a dollar cost using the price of the drug at the time. Refer to Appendix A for additional detail on how the costs were calculated.

What Is the Potential Impact of Voxelotor on State Medicaid Spending?

We estimated that, with 15% uptake and 35% adherence rates and current prices, the total annual cost of voxelotor for treating SCD patients in Medicaid would be $388.1 million nationally (95% confidence bounds, $197.5 million to $794.2 million). This corresponds to a per-member per-month (PMPM) cost of $0.42 (95% confidence bounds, $0.21 to $0.86) for all Medicaid members. Based on the enrollment composition of the SCD patients in CHIP and Medicaid expansion, and the national average of corresponding federal match rates, we estimated that $258.6 million of the total costs will come from

federal funds and the remaining $129.5 million will be paid for by the states. Comparing these estimates against Medicaid total 2022 spending estimates reported elsewhere,[32] voxelotor would potentially account for about 1% of the total Medicaid prescription drug spending.

Exhibit 6 shows the total projected cost estimates for different uptake and adherence scenarios. At the highest uptake and adherence rates (30% and 70%, respectively), the estimated total annual cost of voxelotor is just under $1.1 billion. At the lowest rates of uptake and adherence (5% and 25%, respectively), the estimated total annual cost is about $114 million.

The budget impact of voxelotor on state Medicaid programs varied substantially depending on the SCD prevalence within a state and the size of its Medicaid program. In the 2 states with the fewest members with SCD (Nebraska and Oregon), the overall projected budget impact was less than $1 million. Forecasted voxelotor spending was highest in New York, with estimated spending topping $38 million. On a PMPM basis, the District of Columbia, Georgia, Mississippi had the highest estimated costs of more than $1 PMPM for voxelotor; meanwhile, Colorado, Oregon, and Washington had the lowest estimated PMPM costs, at less than $0.15 for voxelotor (see Appendix F for state budget impact estimates).

CONSIDERATIONS

Voxelotor was approved by the FDA in November 2019 for treatment of SCD (using the accelerated approval pathway), based on the surrogate outcome of increase in Hb. Pfizer, the maker of voxelotor, set a price of $147,389 per year for annual treatment. In September 2024 (almost 5 years later) Pfizer voluntarily withdrew the drug from

EXHIBIT 6

Estimated annual cost of voxelotor (in $M) under different uptake and adherence scenarios

	Uptake (share of eligible Medicaid members)						
Adherence	5%	6.6%	10%	**15%**	20%	25%	30%
25%	114	151	229	343	457	572	686
30%	122	161	244	366	487	609	731
35%	129	171	259	**388**	517	647	776
40%	137	181	274	411	547	684	821
45%	144	191	289	433	577	722	866
50%	152	200	304	456	607	759	911
55%	159	210	319	478	637	797	956
60%	167	220	334	501	668	834	1,001
65%	174	230	349	523	698	872	1,046
70%	182	240	364	546	728	909	1,091

the market, noting that FDA-required postmarket trials showed that the benefits of voxelotor did not outweigh the risks.

The circumstances surrounding the approval and subsequent withdrawal of voxelotor highlight the opportunities and risks of the accelerated approval pathway. In 2012, when enacting the Food and Drug Administration Safety and Innovation Act, Congress identified the role of accelerated approval to "help expedite the development and availability to patients of treatments for serious or life threatening diseases or conditions while maintaining safety and effectiveness standards for such treatments."[33] Sickle cell disease meets the threshold for a life-threatening disease, and voxelotor initially showed promising effects on the Hb surrogate endpoint for treatment of SCD. The FDA and manufacturer agreed upon confirmatory trial endpoints, and the manufacturer took its own action to withdraw the drug from the market due to safety concerns made apparent during those trials.

That said, we estimated that more than 45,000 Medicaid members meet the FDA-indication criteria for voxelotor. While the drug had relatively low uptake following accelerated approval (only 6.6% of Medicaid members with SCD were prescribed voxelotor) more than 2,200 Medicaid members with SCD did end up taking the drug. During the first 2 years on the market (2020 and 2021) alone, Medicaid spent $115 million on voxelotor therapy. Meanwhile, during the nearly 5 years between approval and withdrawal, these 2,200 individuals with SCD were at greater risk for higher rates of VOCs and higher rates of morbidity, due to this drug therapy.

While 5 years to complete the confirmatory trials of voxelotor is longer than the average 3.5 years, the manufacturer has followed Congress's intent for accelerated approval. The manufacturer took its own action to withdraw the drug and did not subject patients, their families, and clinicians to a drawn-out hearing and appeal process with the FDA. Moreover, as our analysis found that the future costs of treatment with voxelotor could cost Medicaid $388 million per year, this voluntary withdrawal will save the states and the federal government from significant unnecessary spending on a drug for which the benefits do not outweigh the risks.

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APPENDIX A

METHODS

See attachment for a full description of the methods used to prepare this brief.

APPENDIX B

MEMBERS WITH AND WITHOUT SCD, 2021

See attachment for this table.

APPENDIX C

DEMOGRAPHIC INFORMATION

See attachment for tables describing the availability of demographic information, and demographic characteristics of Medicaid members included in our study.

EXHIBIT C1
Availability of demographic information for Medicaid members aged 4 to 64 years, 2021

EXHIBIT C2
Demographic characteristics: members with and without sickle cell disease, by age; 2021

EXHIBIT C3
Demographic characteristics: Members with and without sickle cell disease, by sex, 2021

EXHIBIT C4
Demographic characteristics: Members with and without sickle cell disease, by race and ethnicity, 2021

APPENDIX D

HEALTH CARE SERVICE USE

See attachment for tables describing health care service use and medication adherence of Medicaid members included in our study.

EXHIBIT D1
Prevalence of affected body systems and specific conditions in Medicaid members aged 4 to 64 years, 2021

EXHIBIT D2
Health service used by Medicaid members aged 4 to 64 years, 2021

EXHIBIT D3
Health care service use: Hospitalization, 2021

EXHIBIT D4
Health care service use: Intensity of hospital use, 2021

EXHIBIT D5
Health care service use: Emergency department use, 2021

APPENDIX E

VOXELOTOR UPTAKE

See attachment for tables describing voxelotor uptake and use patterns by Medicaid members.

EXHIBIT E1
Voxelotor uptake among eligible Medicaid members with sickle cell disease by state, 2019 to 2021

EXHIBIT E2
Medication adherence, means, and proportions, stratified by enrollment status in the year 2021

APPENDIX F

FORECASTED ANNUAL COST OF VOXELOTOR BY STATE

See attachment for table describing the forecasted annual cost of voxelotor by state.

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