MEDICAID EVIDENCE REVIEW AND COST INITIATIVE BRIEF

Sotorasib (Lumakras) for Non–Small Cell Lung Cancer

OVERVIEW

In 2021, the US Food and Drug Administration (FDA) gave sotorasib (branded as Lumakras) accelerated approval as a treatment for non–small cell lung cancer (NSCLC) when the tumors test positive for the KRAS G12C mutation. Lung cancer is the third most common cancer type in the US[1] and the leading cause of cancer-related deaths in the US.[2,3]

Sotorasib, a molecularly targeted therapy, was given accelerated approval using surrogate clinical endpoints for overall response rate and duration of response.[4] As part of the 2021 approval, the FDA requested a confirmatory trial measuring progression-free survival (PFS) results from a multicenter, randomized clinical trial in participants with locally advanced or metastatic NSCLC.[19]

In 2023, the FDA reviewed results of the manufacturer's confirmatory trial and voted against full drug approval for sotorasib. Instead, the FDA issued a complete response letter allowing the manufacturer to conduct another confirmatory trial, to be completed no later than February 2028. This decision extends the accelerated

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.

approval window to more than 6 years,[23] during which time we estimate that Medicaid may spend approximately $140 million (or $23.1 million per year, assuming no change in the uptake rate) on patient therapy with sotorasib.

What Is Non–Small Cell Lung Cancer?

Lung cancer is broadly divided into 2 main types: small-cell lung cancer, which accounts for approximately 15% of lung cancer cases; and NSCLC, which accounts for the remaining 85% of lung cancer cases.[3,5] Smoking tobacco is the primary risk factor for lung cancer; however, other risk factors, such as exposure to secondhand smoke, occupational hazards (exposure to asbestos, radon, and certain chemicals), air pollution, hereditary cancer syndromes, radiation exposure, and certain chronic lung diseases also are associated with lung cancer.[2,3,6,7]

The most common types of NSCLC include squamous-cell carcinoma (around 25% of all lung cancers), large-cell carcinoma (around 10% of all lung cancers), and adenocarcinoma (around 40% of all lung cancers).[2] Lung cancer may present due to symptoms, be discovered incidentally on chest imaging, or be diagnosed through intentional screening for those with a significant history of tobacco use.[2] Common symptoms include worsening cough, chest pain, coughing up blood

LUNG CANCER and SOTORASIB

OVERVIEW

LUNG CANCER PREVALENCE

IN THE US

In 2024 there will be an estimated 234,580 people newly diagnosed with lung cancer (including NSCLC and small-cell lung cancer), with around 611,000 people living with lung cancer in the US.[9]

IN MEDICAID

70,775 Medicaid members have lung cancer, and 38,733 have metastatic lung cancer. Of these, an estimated 5,732 members may have metastatic or locally advanced NSCLC with KRAS G12C mutation.

SOTORASIB FACTS

DRUG PRICE PER PATIENT

$256,912 per year

FDA ACCELERATED APPROVAL DATE

May 2021; not converted to full FDA approval

MEDICAID COST ESTIMATES

PROJECTED ANNUAL COST TO MEDICAID

National estimate to treat Medicaid members: $23.1 million, with $16.7 million coming from federal funds and $6.4 million from state funds

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 sections about potential Medicaid spending on sotorasib.
Abbreviations. FDA: US Food and Drug Administration; KRAS: Kirsten rat sarcoma viral oncogene homologue; NSCLC: non–small cell lung cancer.

(hemoptysis), fatigue, weight loss, shortness of breath (dyspnea), or hoarseness.[2,8]

Individuals with suspected NSCLC undergo a range of medical investigations to confirm the diagnosis and staging of their disease to determine the disease's extent (e.g., local, regional, or distant).[2] Lung cancer is often diagnosed at an advanced stage, leaving individuals with limited treatment options.[6]

In the US, lung cancer is the third most common cancer type[1] and the leading cause of cancer-related deaths.[2,3] According to the National Cancer Institute, in 2024 there will be an estimated 234,580 new cases of lung cancer (including NSCLC and small-cell lung cancer), and approximately 125,070 deaths from lung cancer.[9] The 5-year relative survival rate for people with lung cancer is 26.7%[9] and varies markedly for individuals diagnosed with local (61%), regional (34%), or distant (i.e., metastatic) stage cancer (7%).[2]

How Is Non–Small Cell Lung Cancer Managed?

At diagnosis, individuals with NSCLC typically are staged using the American Joint Committee on Cancer TNM system based on 3 factors[2]:

1) The size and extent of the primary tumor (T)
2) Involvement of regional lymph nodes (N)
3) The presence or absence of distant (e.g., in bones or brain) metastases (M)

Together, these factors result in a stage category from stage 0 (limited to the lining of the airways) to stage IV (metastatic cancer).[2] Prognosis of the disease is affected by cancer stage, the presence of pulmonary or constitutional symptoms, size of largest tumor(s), metastases to multiple lymph nodes, and vascular invasion.[2]

Treatment options vary depending on the type of lung cancer (e.g., adenocarcinoma, squamous cell carcinoma), the stage at diagnosis, and the general health and function of the individual, and may include radiation therapy, chemotherapy, targeted therapy (e.g., monoclonal antibodies), surgery, or a combination of these.[2] More recently, the identification of genetic mutations in lung cancer has led to the development of molecularly targeted therapies to improve the survival of subsets of individuals with metastatic disease.[2]

Individuals of color living in the US who are diagnosed with lung cancer face worse outcomes compared with individuals who identify as White.[10] Individuals of color are less likely to be diagnosed early, less likely to receive surgical treatment, and more likely receive no treatment.[10] There are also substantial disparities by health insurance status in the use of systemic treatments (drug therapies that work throughout the body) for stage IV NSCLC.[10] In 1 study, individuals with Medicaid or other public insurance were around 22% less likely to receive systemic treatments, around 43% less likely to be treated with bevacizumab, and around 30% less likely to receive tyrosine kinase inhibitors compared with privately insured counterparts.[11]

How Much Does Lung Cancer Cost to Treat?

Non–small cell lung cancer is associated with a considerable economic burden.[12] In 2020, the total cost of lung cancer care in the US was estimated to be $23.8 billion, with $1.8 billion of the total for prescription drugs.[13] Average annual per-patient costs for medical services related to NSCLC were $67,148 for initial care, $12,285 for continuing care, and $109,103 for the last year of life.[13]

Historically, use of health care resources for this condition was driven primarily by hospitalizations and treatments with little or no impact on the disease course or survival.[12,14] Newer treatment options associated with modest gains in survivorship have emerged in recent years; however, these treatments have also driven up overall costs.[12]

SOTORASIB Lumakras®

DRUG SUMMARY

BASIC INFORMATION

DRUG CLASS
Targeted therapy, KRAS protein inhibitor

MANUFACTURER Amgen

PRICE PER PATIENT
$256,912 per year

FDA APPROVAL

PATHWAY Accelerated approval

DATE May 2021

PRESCRIBING LABEL
https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/214665s004lbl.pdf

APPROVED INDICATION(S)

For the treatment of adults with KRAS G12C–mutated locally advanced or metastatic NSCLC, as determined by an FDA-approved companion diagnostic test, who have received at least 1 prior systemic therapy

DOSING

ROUTE Oral

FORMULATION
Tablets

INFORMATION
960 mg orally (three 320-mg tablets or eight 120-mg tablets) once daily until disease progression or unacceptable toxicity

SAFETY

BOXED WARNINGS None

PRECAUTIONS
Hepatotoxicity: Monitor liver function tests every 3 weeks for the first 3 months of treatment then once monthly as clinically indicated. Withhold, reduce dose, or permanently discontinue sotorasib based on the severity.
ILD/Pneumonitis: Monitor for new or worsening pulmonary symptoms. Immediately withhold sotorasib for suspected ILD/pneumonitis and permanently discontinue if no other potential causes of ILD/pneumonitis are identified.

ADVERSE REACTIONS
Diarrhea, musculoskeletal pain, nausea, fatigue, hepatotoxicity, and cough;
Decreased lymphocytes, decreased hemoglobin, increased aspartate aminotransferase, increased alanine aminotransferase, decreased calcium, increased alkaline phosphatase, increased urine protein, and decreased sodium

Sources. IPD Analytics and the US Food and Drug Administration (FDA).
Abbreviations. FDA: US Food and Drug Administration; ILD: Interstitial lung disease; KRAS: Kirsten rat sarcoma viral oncogene homologue; NSCLC: non–small cell lung cancer.

DRUG INFORMATION

In 2021, sotorasib (branded as Lumakras) was approved for the treatment of NSCLC through the FDA accelerated-approval pathway using surrogate clinical endpoints for overall response rate and duration of response.[4] Sotorasib, a molecularly targeted therapy, was specifically approved for the treatment of adults with locally advanced or metastatic NSCLC who test positive for the KRAS G12C mutation, and have received at least 1 prior systemic therapy.[15] Sotorasib is a highly selective KRAS G12C inhibitor and is the first approved therapy for tumors with a *KRAS* gene mutation.[4]

Before starting sotorasib treatment, KRAS G12C mutations should be confirmed by an FDA-approved test.[15] FDA-approved companion diagnostic tests for sotorasib include the Guardant360 CDx blood plasma panel and the Qiagen therascreen KRAS RGQ PCR (polymerase chain reaction) kit for testing tumor tissue samples.[15]

FINDINGS

What Evidence Was Used by the FDA to Approve Sotorasib?

Exhibit 1 is a summary of the study used to approve sotorasib through the accelerated pathway.

EXHIBIT 1

Summary characteristics of the study used to support efficacy of sotorasib

	CodeBreaK 100[17]
Official title	A phase 1/2, open-label study evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of sotorasib (AMG 510) monotherapy in subjects with advanced solid tumors with KRAS p.G12C mutation and sotorasib (AMG 510) combination therapy in subjects with advanced NSCLC with KRAS p.G12C mutation (CodeBreaK 100)
ClinicalTrials.gov ID	NCT03600883
Study design	Single-arm, open-label (nonrandomized, unblinded) trial
Clinical trial phase	Phase 1/2
Study population description	126 adults with locally advanced or metastatic KRAS G12C-mutated NSCLC with disease progression after receiving an immune checkpoint inhibitor or platinum-based chemotherapy, and at least 1 measurable cancerous mass
Patient status requirement	Eastern Cooperative Oncology Group Performance Status 0 or 1
Intervention	Sotorasib, 960 mg orally once per day
Control	No comparator group
Primary outcome used for accelerated approval	Overall response rate and objective response
Trial funding	Amgen and NIH (NCI)

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. KRAS: Kirsten rat sarcoma viral oncogene homologue; NCI: National Cancer Institute; NIH: National Institutes of Health; NSCLC: non–small cell lung cancer.

Why Did the FDA Grant Accelerated Approval?

The FDA considered results from the CodeBreaK 100 study, in which 126 adults with NSCLC received sotorasib.[15] The trial demonstrated a complete response rate (i.e., disappearance of tumor) of 2% and a partial response rate (i.e., smaller tumor size) of 35%.[15] The median duration of objective response (both complete and partial) was 10.0 months (range, 1.3 to 11.1 months), and 58% of participants had a response duration of 6 months or more.[15]

Sotorasib does not have any boxed warning; however, the current prescribing label highlights the warnings and precautions for liver or lung damage (specifically, hepatotoxity and interstitial

EXHIBIT 2

Summary characteristics of the study requested to support full approval

	CodeBreaK 200[18-20]
Official title	A phase 3 multicenter, randomized, open label, active-controlled, study of AMG 510 vs. docetaxel for the treatment of previously treated, locally advanced, and unresectable or metastatic NSCLC subjects with mutated KRAS p.G12C
ClinicalTrials.gov ID	NCT03036813[a]
Study design	Randomized, open-label, active-controlled trial
Study population description	345 adults (aged 18 to 100 years) with previously treated, locally advanced, and unresectable or metastatic NSCLC with KRAS p.G12C mutation confirmed through central testing or have documentation of KRAS p.G12C mutation through previous Amgen study 294 before enrollment
Study arms	2 study arms
Intervention	Sotorasib, 960 mg orally once per day
Control	Docetaxel, 75 mg/m^2 by intravenous infusion every 3 weeks
Study duration	Up to 24 months
Study sites	148 sites located in 22 countries, including the US
Trial funding	Amgen
Primary outcome	Progression-free survival at cutoff date of primary analysis
Outcomes requested by the FDA	Final progression-free survival data
Estimated date of final report submission at the time of accelerated approval	July 2022
Status of requested study	Completed; published in March 2023[19]
Primary completion date	August 2022 (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; KRAS: Kirsten rat sarcoma viral oncogene homologue; NSCLC: non–small cell lung cancer; PMR: postmarketing requirement

lung disease or pneumonitis).[15] The most common adverse reactions (incidence of at least 20%) were diarrhea, musculoskeletal pain, nausea, fatigue, hepatotoxicity, and cough, and the most common laboratory abnormalities (incidence of at least 25%) were decreased lymphocytes, decreased hemoglobin, increased aspartate aminotransferase, increased alanine aminotransferase, decreased calcium, increased alkaline phosphatase, increased urine protein, and decreased sodium.[15]

What Studies Were Requested to Convert Sotorasib to Full Approval?

As part of the accelerated approval in 2021, the FDA requested PFS results from a multicenter, randomized clinical trial in participants with locally advanced or metastatic NSCLC with a history of prior systemic therapy for advanced disease, and whose tumors test positive for the KRAS G12C mutation.[18]

In 2023, the FDA reviewed data from CodeBreaK 200 (NCT04303780) and the committee voted against full approval.[21] The FDA issued a complete response letter calling for another confirmatory study to be completed no later than February 2028.[21,22] As part of the review, the FDA concluded the dose comparison requirement requested at the time of accelerated approval was fulfilled.[21,22] The postmarketing request was to compare the 960-mg dosage with a lower dosage; after

DATA METHODS SUMMARY

Sotorasib is indicated for locally advanced or metastatic NSCLC with KRAS G12C mutation and at least 1 previous treatment. There is no diagnosis code specific to NSCLC and the stage or the genetic variant of the cancer cannot be determined in the claims. Accordingly, researchers at the Center for Evidence-based Policy (Center) used Centers for Medicare & Medicaid Services (CMS) Transformed Medicaid Statistical Information System (T-MSIS) analytic files to identify Medicaid members with lung cancer and metastatic lung cancer, and estimated the percentage of these patients potentially eligible for the treatment based on the literature.

Specifically, we identified members with at least 1 claim with a lung cancer diagnosis (ICD-10 C34) and those with at least 1 claim with the metastasis code (ICD-10 C77-C79) for metastatic lung cancer in addition to a lung cancer diagnosis. We then applied to the lung cancer population the percentages of locally advanced lung cancer, NSCLC, and KRAS G12C mutation obtained from the literature. The initial population for analysis included all Medicaid members aged 64 years or younger. As our focus was on Medicaid expenditures, and members with both Medicaid and Medicare (i.e., dual-eligible) have pharmacy benefits under Medicare Part D, we excluded members with evidence of dual enrollment in the years 2019, 2020, and 2021. Using these criteria, Utah and Alabama were excluded as these states 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 generally did not report data elements for states identified as having unusable or high concern data quality for those elements according to the Data Quality Atlas.

Lung cancer analysis cohorts were anchored in 2021, with a 3-year look-back period to ensure comprehensive Medicaid member identification. Health care service use and comorbidities among lung cancer patients was compared with the Medicaid-insured population overall using a 3-to-1 exact matching method based on state, age (in years), sex, and race/ethnicity. Our utilization metrics do not have a continuous enrollment requirement. Our cost model estimated annual cost for the drug from a payer perspective using inputs of drug indication prevalence, drug uptake, and average treatment duration observed in T-MSIS data and in the literature, as well as reported drug acquisition costs and statutorily required rebates. Refer to Appendix A for additional detail on how we conducted this study.

reviewing the data, the FDA retained approval for the higher 960-mg dosage.[21,22] However, this decision is not without controversy. Concerns have been raised about the design of the CodeBreaK 200 study and the new requested study (CodeBreaK 202, NCT05920356), as well as retaining approval for the higher dose.[23-25] In the dose-comparison study, no differences were seen in PFS or overall survival between the 960 mg and 240 mg doses; however, there were fewer side effects with the lower dose.[23-25] At the time of writing this report, sotorasib has not converted to full FDA approval.[26]

How Common Is Lung Cancer Among Medicaid Members?

Our analytic cohort included 82,885,834 Medicaid members aged 0 through 64 years who were not dually eligible in 2021 (members in Alabama and Utah were excluded because of data availability). Of these, 70,775 (8.5 per 10,000 members) were identified as having lung cancer and 38,733 (4.7 per 10,000 members) as having metastatic lung cancer.

Lung cancer was most common among non-Hispanic White, non-Hispanic Black, and

EXHIBIT 3

Characteristics of Medicaid members with and without lung cancer, 2021

	with metastatic lung cancer[a]	%[b]	with any lung cancer[a]	%[b]	without any lung cancer[a]	%[b]
Total members	*38,733*	-	*70,775*	-	*82,885,834*	-
Age, in years						
0 to 44	3,648	9.4	8,164	11.5	69,577,644	83.9
45 to 54	8,439	21.8	14,087	19.9	6,533,733	7.9
55 to 64	26,646	68.9	47,953	67.8	6,602,611	8.0
Sex						
Female	19,193	49.6	36,726	52.3	44,372,568	54.1
Male	19,243	49.8	33,477	47.7	37,638,184	45.9
Race and ethnicity						
American Indian or Alaska Native, non-Hispanic	277	1.0	498	1.0	875,026	1.5
Asian, non-Hispanic	1,013	3.8	1,679	3.5	2,391,406	4.2
Black, non-Hispanic	5,289	19.9	9,563	20.0	11,844,289	20.8
Hispanic	2,647	10.0	4,598	9.6	17,091,088	30.1
Native Hawaiian or Pacific Islander, non-Hispanic	80	< 1	144	< 1	275,320	< 1
White, non-Hispanic	17,069	64.3	31,062	64.9	26,636,380	41.6
Multiracial, non-Hispanic	94	< 1	202	< 1	551,883	1.0
Other race or ethnicity	75	< 1	113	< 1	194,080	< 1

Notes. [a] Excluding dually eligible members and members in Utah and Alabama. [b] Percentage of members without missing data on demographic characteristics. There were 47,849 (67.6%) members with lung cancer and 56,855,472 (68.6%) members without lung cancer who had no missing race/ethnicity data. For more detail see Appendix B.

Hispanic Medicaid members (64.9%, 20% and 10%, respectively; Exhibit 3). More than two-thirds (67.8%) of lung cancer patients were aged 55 years or older and only 11.5% were younger than age 45. The demographic composition of metastatic lung cancer patients was similar.

Lung cancer prevalence varied among state Medicaid populations, from around 4 cases per 10,000 members in South Dakota, to more than 16 cases per 10,000 members in Ohio and West Virginia. Lung cancer was most common in some Midwestern and Northeastern states, with West Virginia, Ohio, Kentucky, Maine, Missouri, Pennsylvania, Vermont, Michigan, New Hampshire, and Indiana experiencing lung cancer rates higher than 11 cases per 10,000 members (Exhibit 4). This pattern was largely similar for the prevalence of metastatic lung cancer (see Appendix C for state prevalence).

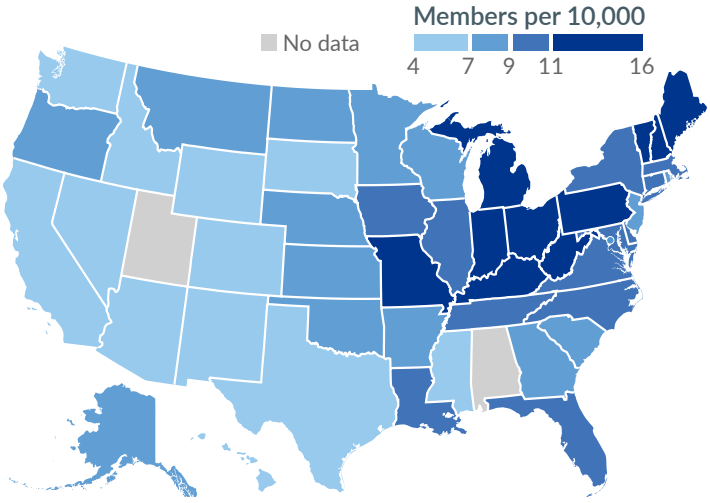
How Do Medicaid Members With Lung Cancer Compare With Sotorasib Trial Populations?

The demographic characteristics of patients included in the drug trials varied somewhat from our Medicaid cohort. While both the sotorasib study cohort and Medicaid cohorts were primarily White, the study cohorts were more predominantly so (81.7% in the trial compared with 64.9% in Medicaid). Fifteen percent of the sotorasib cohort were Asian, compared with 3.8% of the Medicaid cohort. Both the sotorasib study cohort and Medicaid cohort ages were largely comprised of older adults with a mean age of 63.5 years in the sotorasib trial, while more than 68% of the Medicaid cohort was older than the age of 55.

Exhibit 5 describes the prevalence of body system–level impairments (as defined by the Chronic Illness and Disability Payment System methodology) for Medicaid members aged 64 years old or younger with metastatic lung cancer compared with members without any lung cancer (matched 1:3 on state, age, sex, and race and ethnicity) identified in 2021 Medicaid claims.

EXHIBIT 4

Lung cancer prevalence in Medicaid per 10,000 members, by state, 2021



Note. Data not available for Alabama and Utah.

EXHIBIT 5

Prevalence of affected body systems in Medicaid members with and without metastatic lung cancer, 2021

	Medicaid members with metastatic lung cancer		Matched Medicaid members without metastatic lung cancer	
System or condition	N	%[a]	N	%[a]
Total members[a]	*38,272*	-	*111,816*	-
Cardiovascular	24,198	63.2	44,779	39.1
CNS	8,840	23.1	9,823	8.6
Gastrointestinal	12,693	33.1	16,838	14.7
Infectious disease	9,920	25.9	7,065	6.2
Metabolic	14,310	37.4	7,247	6.3
Musculoskeletal	8,950	23.4	17,587	15.3
Psychiatric	8,640	22.6	19,869	17.3

Note. [a] Members included in this calculation are those with at least 1 inpatient or 1 outpatient claim in 2021. There were 461 members with metastatic lung cancer who did not have any Medicaid claims in 2021 and were eliminated from this calculation along with their matched comparisons.
Abbreviation. CNS: central nervous system.

A larger proportion of members with metastatic lung cancer had comorbid conditions across all body systems than their matched comparisons. Although cardiovascular conditions were most common among both groups, 63.2% of members with metastatic cancer were affected by this condition compared with 39.1% of their matched comparisons. More than one-third of members with metastatic cancer had pulmonary, metabolic, and gastrointestinal conditions; 15% or fewer of their matched counterparts had those conditions.

Members with metastatic lung cancer had substantially higher hospital and emergency department use than their matched comparisons (Exhibit 6). Specifically, 57.4% of Medicaid members with metastatic lung cancer experienced at least 1 hospitalization in 2021, compared with 11.7% of members without metastatic lung cancer. Members with metastatic lung cancer also experienced more total inpatient days (8,260 vs. 1,379 per 1,000 members), were more likely to experience hospital stays lasting at least 5 days (37% vs. 6%), and had higher emergency department use across multiple measures.

How Common Was Sotorasib Use Among Medicaid Members in 2021?

Sotorasib was approved in May 2021. In the last 7 months of 2021, we identified 167 members with claims for sotorasib (Exhibit 7). We estimated that 2.9% to 4.6% of eligible patients in 2021 received the drug (see Methods Appendix for detail).

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

Due to provisions of the Omnibus Budget Reconciliation Act of 1990, which established the Medicaid Drug Rebate Program, state Medicaid programs must cover FDA-approved drugs if the manufacturer signed a rebate agreement with US Department of Health and Human Services. Therefore, FDA approval, including accelerated

EXHIBIT 6

Health service use by matched Medicaid members with and without metastatic lung cancer, 2021

	Members with metastatic lung cancer[a]	Matched members without lung cancer[a]
Total members	*38,733*	*116,199*
Hospitalizations		
% with ≥ 1 hospitalization	57.4	11.7
% with ≥ 2 hospitalizations	30.9	4.0
Total hospitalizations, per 1,000 members	1,241	203
Total inpatient days, per 1,000 members	8,260	1,379
Average length of stay per hospitalization, days	6.7	6.8
% with ≥ 1 hospitalization lasting ≥ 5 days	37.0	6.0
Emergency visits		
% with ≥ 1 ED visit	67.8	31.0
% with ≥ 5 ED visits	12.7	3.1
Total ED visits per 1,000 members	2,096	728

Note. [a] Medicaid members without metastatic lung cancer matched to members with metastatic lung cancer at 3:1 on state of residence, age, sex, race, and ethnicity.
Abbreviations. ED: emergency department.

EXHIBIT 7

Sotorasib users compared with all lung cancer patients in Medicaid, 2021

	Sotorasib users[a]		All other members with lung cancer[a]	
	N	%[b]	N	%[b]
Total members	*167*	-	*70,618*	-
Age, in years				
0 to 44	12	7.2	8,196	11.6
45 to 54	40	24.0	14,163	20.1
55 to 64	115	68.9	48,259	68.3
Sex				
Female	103	63.2	36,627	52.3
Male	60	36.8	33,423	47.7

Notes. [a] Excluding dually eligible members and members in Alabama and Utah. [b] Percentage of members without missing data on demographic characteristics.

approval, is a key factor in establishing the requirement for Medicaid coverage. We estimate that, with an uptake rate of 4% and an average treatment duration of 6 months, the total annual cost of sotorasib for NSCLC treatment in Medicaid to be $23.1 million (95% confidence bounds, $7.9 million and $44.1 million). This corresponds to a per-member per-month (PMPM) cost of $0.02 (95% confidence bounds, $0.01 and $0.05) for all Medicaid members. Based on the enrollment composition of the lung cancer patients in CHIP (Children's Health Insurance Program) and Medicaid expansion, and the weighted national average of corresponding federal match rates, we estimated $16.7 million of the total costs would come from federal funds and the remaining $6.4 million would be paid for by the states.

The number of patients eligible for the treatment and the uptake rate used in cost calculations are based on the lung cancer prevalence and sotorasib uptake observed in 2021 Medicaid data and inputs from the literature and other sources. When we further restricted the eligible members to those with at least 1 claim for a prior systematic therapy, the estimated annual costs were $19.9 million nationally (95% confidence bounds, $7.2 million and $43.9 million). Refer to the Methods Appendix (Appendix A) for additional detail on model inputs and assumptions.

Exhibit 8 shows the total projected cost estimates for different uptake and average treatment duration scenarios. At the highest uptake rate and average treatment duration (8% and 9 months, respectively), the estimated total annual cost of sotorasib is more than $69 million. At the lowest rates of uptake rate and average treatment duration (1% and 3 months, respectively), the estimated total annual cost is about $3 million.

CONSIDERATIONS

According to the National Cancer Institute, in 2024 there will be an estimated 234,580 new cases of lung cancer (including both NSCLC and small-cell lung cancer), and an estimated 125,070 deaths from lung cancer.[9] Our analysis of nondually eligible Medicaid members aged 64 and younger in 2021 identified 70,775 as having lung cancer and 38,733 as having metastatic lung cancer. Lung cancer is often diagnosed at an advanced stage, leaving individuals with limited treatment options.[6] The identification of genetic mutations in lung cancer led to the development of molecularly targeted therapies, such as sotorasib, to improve the survival of subsets of individuals with metastatic disease.[2]

In 2021, sotorasib (branded as Lumakras) was approved for the treatment of NSCLC through the FDA's accelerated approval pathway using surrogate clinical endpoints for overall response rate and duration of response.[4] It is a highly selective KRASG12C inhibitor[4] and we estimated there were 5,732 Medicaid members in 2021 who had metastatic or locally advanced NSCLC with the KRAS G12C mutation.

In 2023, the FDA reviewed results of the manufacturer's confirmatory trial and voted against

EXHIBIT 8

Estimated annual cost of sotorasib (in $M) under different uptake and average treatment duration scenarios

Average treatment duration (months)	Uptake (share of eligible Medicaid members)							
	1%	2%	3%	**4%**	5%	6%	7%	8%
3	3	6	9	12	14	17	20	23
4	4	8	12	15	19	23	27	31
5	5	10	14	19	24	29	34	38
6	6	12	17	**23**	29	35	40	46
7	7	13	20	27	34	40	47	54
8	8	15	23	31	38	46	54	61
9	9	17	26	35	43	52	61	69

full drug approval for sotorasib. Instead, the FDA issued a complete response letter allowing the manufacturer to conduct another confirmatory trial to be completed no later than February 2028. This decision extends the accelerated approval window to more than 6 years,[23] during which time we estimate that Medicaid may spend approximately $140 million (or $23.1 million per year, assuming no change in the uptake rate) on patient therapy with sotorasib.

This extended window for accelerated approval also allows the manufacturer to maintain the drug label dosage at 960 mg despite evidence that a lower dosage of 240 mg may have similar clinical outcomes and fewer side effects.[25,27] With the significant benefits to patients, it is unclear why the manufacturer has not requested FDA approval of a dose change for sotorasib's label. It is possible there are adverse financial incentives for the manufacturer to lower the dosage amount and receive a lower payment for a patient course of treatment.[28,29]

While state and federal policymakers wait for the results of sotorasib's second confirmatory trial, they will need to budget for ongoing costs of treatment and consider options to allow dose levels lower than the FDA-approved label. This question of dose optimization is particularly important for state policymakers as many states have a requirement to abide by the FDA label or a recognized drug compendium. State and federal policymakers may want to share information about dose optimization for sotorasib with patients and clinicians to support decision making about appropriate treatment.

PROJECT TEAM

RHONDA ANDERSON, RPH
Director of Pharmacy

MARCUS BACHHUBER, MD, MSHP
Clinical Epidemiologist

CAITLIN BURBANK, PT, PHD
Research Associate III

GÜLCAN ÇIL, PHD
Senior Statistician

GALEN GAMBLE, BA
Project Coordinator

DAVID RADLEY, PHD, MPH
Research Director, Data and Analytics

MOIRA RAY, MD, MPH
Clinical Epidemiologist

JENNIFER RYAN, ND, MS, CCRP
Research Associate II

BETH SHAW, MSC
Research Director, Evidence Synthesis

SUSAN STUARD, MBA
Director, State Technical Assistance

SNEHA YEDDALA, PHARM D, MS
Research Associate I

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APPENDIX A

METHODS

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

EXHIBIT A1

Cost-modeling inputsfor all metastatic and locally advanced NSCLC patients

EXHIBIT A2

Cost-modeling inputs for matastatic and locally advanced NSCLC patients with prior treatment

APPENDIX B

DEMOGRAPHIC INFORMATION

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

APPENDIX C

MEDICAID MEMBERS WITH AND WITHOUT LUNG CANCER, 2021

See attachment for this table.

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centerforevidencebasedpolicy.org

Center for Evidence-based Policy

3030 South Moody Avenue, Suite 250
Portland, OR 97201

Phone: (503) 494-2182
Fax: (503) 494-3807

centerforevidencebasedpolicy.org