MERCI Brief
April 2025

MEDICAID EVIDENCE REVIEW AND COST INITIATIVE BRIEF

Onasemnogene Abeparvovec-xioi (Zolgensma) for Spinal Muscular Atrophy

OVERVIEW

Spinal muscular atrophy (SMA) is a group of serious genetic conditions, usually presenting in childhood, categorized by progressive muscle weakness and loss of movement.[1,2] Ultimately, disease progression results in impairments in breathing and swallowing, which can lead to death as early as age 2 in children with type 1 SMA.[1] SMA is caused by reduced production of a key protein in survival motor neurons (SMN).[1,2] Onasemnogene abeparvovec-xioi (branded as Zolgensma) was developed as a gene therapy to deliver a functional copy of the *SMN1* gene into children under 2 years of age, restoring protein production and motor neuron function.[2-4]

Zolgensma received Food and Drug Administration (FDA) approval based on 2 trials in a total of 36 children; these trials demonstrated that based on comparisons with historical controls, Zolgensma may delay death or permanent ventilation.[4] In the second trial of high-dose versus low-dose Zolgensma, outcomes were further improved in the high-dose group, which the FDA

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.

determined supported efficacy by demonstration of a dose-response relationship.[4] Long-term outcomes beyond 18 to 24 months are currently under study.[5]

Zolgensma has a very high cost per dose ($2.125 million). In our analysis of Medicaid data from May 2019 through 2021, we identified 146 Medicaid members who received Zolgensma. We estimated the cost to have been $276.2 million, with an estimated $101.1 million coming from state funds. Zolgensma expenditures can represent a large and potentially unaffordable line item within an already stretched Medicaid pharmacy budget.

Zolgensma may represent a potentially successful one-dose treatment for a previously fatal genetic disease. However, due to the relatively small studies that led to its approval, the full scope and magnitude of the benefits and harms of Zolgensma are not yet known. State Medicaid administrators might consider their coverage criteria of Zolgensma, including limiting coverage to align with the clinical trial criteria, as opposed to the broader FDA approval. Further, state Medicaid staff can monitor for evidence of long-term efficacy, and examine health care usage after Zolgensma administration, to allow for accurate planning of future expenditures related to SMA.

What Is Spinal Muscular Atrophy?

Spinal muscular atrophy (SMA) is a group of hereditary diseases which affect the nerve cells that control voluntary muscles (motor neurons).[1,2] SMA is caused by genetic variants resulting in lowered production of a key protein (SMN), with the level of SMN correlating with the severity of the patient's SMA disease course.[6]

People with SMA experience progressive muscle weakness and loss of movement due to muscle wasting (atrophy) and loss of motor neurons.[1] The

SPINAL MUSCULAR ATROPHY (SMA) and ONASEMNOGENE ABEPARVOVEC-XIOI

OVERVIEW

SMA PREVALENCE

IN THE US

The incidence of SMA is from 5 to 13 per 100,000 live births.[3,7,9]

IN MEDICAID

Out of 6 million Medicaid members aged under 2 years in 2021, 459 were identified as having SMA.

ONASEMNOGENE ABEPARVOVEC-XIOI FACTS

DRUG PRICE PER PATIENT $2,391,706 per one-time treatment

FDA ACCELERATED APPROVAL DATE May 2019

MEDICAID COST ESTIMATES

PROJECTED ANNUAL COST TO MEDICAID

$158.9 million, with $93.5 million coming from federal funds and $65.4 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 section about potential Medicaid spending on Zolgensma
Abbreviations. SMA: spinal muscular atrophy; FDA: US Food and Drug Administration.

weakness in skeletal muscles affects functions like walking, sitting, arm movement, and head control.[1,2] In many types of SMA, disease progression also leads to difficulty breathing and swallowing, ultimately resulting in an inability to breathe without mechanical ventilation and death at an early age.[1]

SMA classification is based on age at symptom onset and maximum motor function achieved.[2] The traditional classification includes:

- **Type 0:** This is a very rare and severe type of SMA that affects < 1% of children with SMA,[7] with symptoms beginning prior to birth.[2] At birth, the infant has severe weakness and difficulty breathing and feeding.[2]
- **Type 1:** This type (also known as infantile-onset SMA) is the most common form of SMA,[2] affecting approximately 45% of children with SMA.[7,8] Symptoms usually become apparent before 6 months of age.[2] and include severe muscle weakness and difficultly coughing, breathing, and swallowing.[2]
- **Type 2:** Symptoms typically appear between 6 and 18 months of age,[2] affecting 20% of children with SMA.[7] Children have the ability to sit without support but are unable to stand or walk without help.[2]
- **Type 3:** This type usually shows with symptoms after 18 months of age,[2] affecting 30% of children with SMA.[7] Children with type 3 experience difficulty in walking independently, running, rising from a chair, or climbing stairs.[2]
- **Type 4:** Symptoms develop after 18 years of age affecting < 5% of patients with SMA,[7] with mild to moderate leg muscle weakness and other symptoms.[2]

How Many People Have Spinal Muscular Atrophy in the US?

Genetic carrier screening before or during pregnancy helps detect pathogenic *SMN1* gene variant carriers.[2,9] Newborn screening can help identify SMA before symptoms develop, with the aim of improving early therapeutic intervention and ultimately improving patient and clinical outcomes.[7,10]

The incidence of SMA is from 5 to 13 per 100,000 live births.[3,7,9] Between 2018 and 2022, newborn screening across 30 states identified 425 infants who screened positive and had a confirmed diagnosis of SMA, leading to an estimate birth prevalence of SMA of 1 in 14,694 live births in the US.[11]

How Is Spinal Muscular Atrophy Managed?

There are currently 3 FDA-approved disease-modifying therapies for SMA,[3] each of which aims to preserve motor neurons, improve muscle function, and increase life expectancy[2,7]:

- Nusinersen (Spinraza): An intrathecally administrated drug to treat SMA in children and adults.[2]
- Onasemnogene abeparovec-xioi (Zolgensma): A gene therapy administered as an intravenous infusion for children under 2 years of age with SMA type 1 with biallelic mutations in the *SMN1* gene.[2-4]
- Risdiplam (Evrysdi): An oral medication for children aged 2 months or older.[2]

Other supportive therapies include nutrition, physical therapy, occupational therapy, and rehabilitation to help patients improve posture, prevent joint immobility, and slow muscle weakness.[2]

An exploratory study conducted using a US-based claims dataset found the disease burden of SMA extends beyond the neuromuscular degenerative symptoms associated with SMA[12]; this finding emphasizing the need for early and effective identification of SMA.

Gene therapies for SMA are most effective when administered before symptoms appear, emphasizing the importance of newborn screening.[13] All US states now include testing for SMA type 1 in their routine newborn screening.[14,15]

ONASEMNOGENE ABEPARVOVEC-XIOI Zolgensma®

DRUG SUMMARY

BASIC INFORMATION

DRUG CLASS
Recombinant AAV-9 gene therapy

MANUFACTURER
Novartis Gene Therapies

PRICE PER PATIENT (2025)
$2,391,706 per one-time treatment

DOSING

ROUTE Intravenous (IV)

FORMULATIONS
Single-dose vial for IV infusion

INFORMATION
1.1×10^{14} vg/kg (vector genomes per kg of body weight)

APPROVED INDICATION(S)

Treatment of spinal muscular atrophy (SMA) in pediatric patients less than 2 years of age with biallelic mutations in the survival motor neuron 1 (*SMN1*) gene

FDA APPROVAL

PATHWAY
Gene therapy; Center for Biologics Evaluation and Research (CBER) product approval

DESIGNATIONS
Fast track, breakthrough therapy, priority review, and orphan drug

DATE May 2019

PRESCRIBING LABEL
https://www.fda.gov/vaccines-blood-biologics/zolgensma

SAFETY

BOXED WARNINGS
Serious liver injury and acute liver failure
Prior to infusion, assess liver function of all patients by clinical examination and laboratory testing. Administer systemic corticosteroid to all patients before and after infusion. Continue to monitor liver function for at least 3 months after infusion, and at other times as clinically indicated.

PRECAUTIONS

- Administer Zolgensma to patients who are clinically stable in their overall baseline health status (e.g., hydration and nutritional status, absence of infection) prior to infusion.
- Monitor platelet counts before infusion, and at least weekly for the first month and then every other week for the second and third month or until platelet counts return to baseline.
- Prompt attention to signs and symptoms of thrombotic microangiopathy (blood clots in small blood vessels) is advised, as this can result in life-threatening or fatal outcomes. If clinical signs, symptoms and/or laboratory findings occur, consult a pediatric hematologist and/or pediatric nephrologist immediately to manage as clinically indicated.
- Monitor troponin-I (a marker of heart muscle damage) before infusion, and weekly for the first month and then monthly for the second and third month until troponin-I level returns to baseline.
- There is a theoretical risk of tumorigenicity due to integration of AAV vector DNA into the genome. Report cases of tumors in patients who received Zolgensma to Novartis Gene Therapies, Inc.

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).

How Much Does It Cost to Treat Spinal Muscular Atrophy?

As of 2020, the annual average estimated treatment costs for patients with SMA type 1 ranged from $75,047 to $196,429 ($92,414 to $241,887 in 2025 US dollars[16]).[17] The treatment costs variability accounts for the fact that life expectancy for many patients with SMA is 2 years or less.

The wholesale acquisition costs of the medications indicated for SMA are: $426,113/year for Spinraza, $409,650/year for Evrysdi, and a one-time treatment cost of $ 2,391,706 for Zolgensma.[18]

DRUG INFORMATION

In 2019, the FDA approved onasemnogene abeparvovec-xioi (branded as Zolgensma) for the treatment of pediatric patients under 2 years of age with SMA and pathogenic variants in both copies of the *SMN1* gene.[4] The approval was based on survival and achievement of developmental motor milestones, such as sitting without support.[4]

The FDA granted fast track, breakthrough therapy, and priority review designations to Zolgensma to expedite its approval process.[19] Additionally, the FDA assigned Zolgensma orphan drug and rare pediatric disease designation.[19]

Zolgensma delivers a functional copy of the *SMN1* gene using an AAV9 vector.[19] The viral vector carries the gene into motor neurons, where the body produces SMN protein, to help restore motor neuron function.[19]

FINDINGS

What Evidence Was Used by the FDA to Approve Zolgensma?

The FDA approval was based on data from 2 open-label, single-arm clinical studies: 1 completed, and 1 ongoing at the time.[4,19] Both studies included participants under 2 years of age with SMA and who had bi-allelic mutations in the *SMN1* gene and 2 copies of the *SMN2* gene.[4] Zolgensma was administered as a single-dose intravenous infusion over 30 to 60 minutes.[4]

What was the effectiveness of Zolgensma at the time of FDA approval?

Study 1 (STR1VE; NCT03306277) enrolled 21 participants, none of whom needed a ventilator support or a feeding tube.[4] The mean age of the participants at the time of treatment was 3.9 months (range, 0.5 to 5.9 months).[4] All the participants received a single dose of 1.1×10^{14} vg/kg (vector genomes per kg of body weight) of Zolgensma.[4]

The efficacy of the drug was evaluated based on survival, defined as the time from birth to either death or permanent ventilation, and the achievement of developmental motor milestones, such as sitting without support.[4] Interim data from the ongoing study showed that 19 participants were alive without permanent ventilation.[4] Thirteen of the 19 participants reached 14 months of age without permanent ventilation and continued in the trial.[4] The ability to sit without support for at least 30 seconds was achieved by 10 participants, with a mean age of 12.1 months.[4] Sixteen (76%) participants were not dependent on noninvasive ventilators at 14 months.[4] The study did not include a contemporaneous comparison group; however, based on natural history only around 25% of untreated patients would be expected to reach the milestones of being alive and not using permanent ventilation beyond 14 months of age.[4]

Study 2 (NCT002122952) enrolled 15 patients in 2 treatment cohorts (low-dose and high-dose).[4] The low-dose (6.7×10^{13} vg/kg)[20] cohort included 3 participants with a mean age of 6.3 months (range, 5.9 to 7.2 months) at the time of treatment and the high-dose cohort (2×10^{14} vg/kg)[20] included 12 participants with a mean age of 3.4 months (range, 0.9 to 7.9 months).[4] For reference, the participants in the low-dose cohort received around one-third of the higher dose.[4]

After 24 months of follow-up, all 12 participants in the high-dose cohort were alive without permanent ventilation; in the low-dose cohort, all 3 participants were alive, with 1 participant requiring permanent ventilation.[4] In the high-dose cohort, 9 participants were able to sit without support for at least 30 seconds and 2 participants were able to stand and walk without assistance.[4]

None of the participants in the low-dose cohort achieved these milestones.[4] The FDA noted that the high-dose cohort showed the dose-response relationship and supported the effectiveness of Zolgensma.[4]

Exhibit 1 provides a summary of the studies used to approve Zolgensma.

EXHIBIT 1

Summary characteristics of the studies used to support approval of Zolgensma[4,21-24]

	Study 1 (STR1VE)	Study 2
Official title	Phase 3, open-label, single-arm, single-dose gene replacement therapy clinical trial for patients with spinal muscular atrophy type 1 with 1 or 2 *SMN2* copies delivering AVXS-101 by intravenous infusion	Phase 1 gene transfer clinical trial for spinal muscular atrophy type 1 delivering AVXS-101
ClinicalTrials.gov ID	NCT03306277	NCT02122952
Study design	Single-arm, open-label, single-dose study	Open-label, single-arm, dose-escalation study
Clinical trial phase	Phase 3	Phase 1
Study population description	Participants with symptomatic or pre-symptomatic SMA type 1, with a disabling mutation of *SMN1* and 1 or 2 copies of *SMN2*	Participants with genetically confirmed diagnosis of SMA type 1, homozygous *SMN1* exon 7 deletions, and 2 copies of *SMN2*
# of study participants (total)	22	15
# of study participants assigned to Zolgensma group	22 included in the primary intention-to-treat analysis, 19 participants completed the trial	3 participants in the low-dose cohort and 12 in the high-dose cohort
Age of participants	Mean age (SD): 3.7 (1.6) months	Mean age in low-dose cohort: 6.3 (range, 5.9 to 7.2) months Mean age in high-dose cohort: 3.4 (range, 0.9 to 7.9) months
Vaccinations	Had to be up-to-date on childhood vaccinations, including seasonal vaccinations	Recommended to follow all routinely scheduled vaccinations, including seasonal vaccinations
Motor function evaluation	Swallowing evaluation test performed prior to administration of gene replacement therapy	Hypotonia and muscle weakness at the time of enrollment

	Study 1 (STR1VE)	Study 2
Prophylactic measures for elevated liver enzymes	Participants received prednisolone (1 mg/kg per day), beginning 24 h before the infusion up to 30 days or more after the infusion	Participants received prednisolone (1 mg/kg per day), beginning 24 h before the gene vector infusion up to 30 days or more after the infusion
Study arms	1 study arm	1 study arm, 2 dose cohorts
Intervention	One-time intravenous infusion of 1.1×10^{14} vg/kg Zolgensma for 30 to 60 minutes via a peripheral vein	One-time intravenous infusion of 6.7×10^{13} vg/kg or 2×10^{14} vg/kg Zolgensma for approximately 60 minutes
Control	No comparator group	No comparator group
Co-primary outcomes	Survival, defined as the absence of death or permanent ventilation Functional, independent sitting for 30 seconds	Safety, defined as any treatment-related adverse events of grade 3 or higher
Secondary endpoints	Ability to thrive at age 18 months, defined as a composite of swallowing function, nutritional support, and weight maintenance Independence from ventilation support	Time until death or permanent ventilation Change in motor function
Study duration	Up to 18 months	Up to 24 months pontinfusion
Study sites	16 locations in US	1 location in US
Trial funding	Novartis Gene Therapies	AveXis, Sophia's Cure Foundation, Research Institute at Nationwide Children's Hospital

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. SD: standard deviation; SMA: spinal muscular atrophy; SMN: survival motor neuron (gene); vg: vector genome(s).

What was the known safety profile of Zolgensma at the time of FDA approval?

The FDA issued a boxed warning for Zolgensma, highlighting it may cause serious liver injury and acute liver failure[4]:

- Acute liver failure leading to death has been reported
- Acute liver injury and elevated aminotransferases can also occur
- Patients with preexisting liver impairment may be at higher risk

The FDA recommended that clinicians[4]:

- Assess liver function for all patients by clinical examination and laboratory testing prior to infusion
- Administer corticosteroids to all patients before and after infusion
- Continue to monitor liver function for at least 3 months after infusion and at other times as clinically indicated

EXHIBIT 2

Characteristics of Medicaid members aged 0 to 2 with and without SMA, 2021

	with SMA[a]	%[b]	without SMA[a]	%[b]
Total members	*459*	-	*5,948,018*	-
Age, in years				
0	131	28.5	1,765,102	29.7
1	177	38.6	2,067,101	34.8
2	151	32.9	2,115,815	35.6
Sex				
Female	215	47.4	2,909,554	48.9
Male	239	53.6	3,038,230	52.1
Race and ethnicity				
Black, non-Hispanic	36	14.2	772,511	22.3
Hispanic	79	31.2	1,133,884	32.7
White, non-Hispanic	122	48.2	1,324,920	38.2
All other race or ethnicity, non-Hispanic	16	6.3	235,507	6.8

Notes. [a] Excluding dually eligible members and members in Alabama, Mississippi, and Utah. [b] Percentage of members with nonmissing data on demographic characteristics. 55.1% of the members SMA and 58.3% of the members without SMA had nonmissing race or ethnicity data. For more detail see Appendix B.
Abbreviation. SMA: spinal muscular atrophy.

How Common Is Spinal Muscular Atrophy Among Medicaid Members?

Our analytic cohort included 5,948,018 Medicaid members aged under 2 years at any point in 2021 who were not dually eligible in 2021. Of these, we identified 459 (7.7 per 100,000 members aged under 2 years) as having SMA, with their first SMA claim before their second birthday.

Among Medicaid enrollees identified with SMA, 48.2% identified as non-Hispanic White, 31.2% as Hispanic, and 14.2% as non-Hispanic Black (Exhibit 2).

How Do Medicaid Members With SMA Compare With Zolgensma Trial Populations and Other Medicaid Members?

The demographic characteristics of children included in the drug trials varied from our Medicaid cohort. Only 18% of the STR1VE trial cohort were Hispanic, while 31.2% of Medicaid members with SMA are Hispanic.[23] In the STR1VE and Study 2 trials, females made up a higher percentage of participants (55% and 60%, respectively) than is seen in Medicaid members with SMA (only 47% female).[23,24] The demographic characteristics of the trial participants are summarized in Appendix C.

Medicaid members with SMA had substantially higher hospital and emergency department use than matched Medicaid members without SMA (Exhibit 3). Specifically, 46.2% of Medicaid members with SMA experienced at least 1 hospitalization in 2021, compared with 23.7% of members without SMA. Members with SMA also experienced many more total inpatient days (12,011 vs. 1,078 per 1,000 members), were more likely to experience hospital stays lasting at least 5 days (25.1% vs. 3.3%), and had higher emergency department use (1,885 vs. 654 visits per 1,000 members).

EXHIBIT 3

Health service use by matched Medicaid members with and without SMA, 2021

	Members with SMA	Matched members without SMA[a]
Total members	*459*	*1,377*
Hospitalizations		
% with ≥ 1 hospitalization	46.2	23.7
% with ≥ 2 hospitalizations	21.6	1.9
Total hospitalizations, per 1,000 members	1,346	264
Total inpatient days, per 1,000 members	12,011	1,078
Average length of stay per hospitalization, days	8.9	4.1
% with ≥ 1 hospitalization lasting ≥ 5 days	25.1	3.3
Emergency visits		
% with ≥ 1 ED visit	50.3	34.9
% with ≥ 5 ED visits	9.4	1.7
Total ED visits, per 1,000 members	1,885	654

Note. [a] Medicaid members without SMA matched to members with SMA at 3:1 on state, age, sex, race, and ethnicity.
Abbreviations. ED: emergency department; SMA: spinal muscular atrophy.

DATA METHODS SUMMARY

Zolgensma is a gene therapy used for SMA. 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 who are potentially eligible for this treatment.

Specifically, we identified members aged 2 years or younger with at least 1 inpatient or at least 2 outpatient claims with a SMA diagnosis (ICD-10 codes G12.0, G12.1, G12.8, and G12.9). As our focus was Medicaid expenditures, we excluded members with evidence of dual enrollment (members with both Medicaid and Medicare coverage), as dually eligible members also have pharmacy benefits under Medicare Part D. Using these criteria, data from Alabama and Utah were excluded as these states do not report dual-enrollment status. 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 (e.g., race or ethnicity) for states identified as having "unusable" or "high concern" data quality according to Data Quality Atlas. Due to unusable data quality for procedure codes in institutional outpatient claims submitted in Illinois and New York, we excluded those 2 states from the analysis of members with Zolgensma claims.

To identify those who are potentially eligible for the treatment in 2021, we focused on members with SMA who were younger than 2 years old at any point during the year (i.e., had their second birthday in 2021 or later including those who were born in 2021). We excluded a small number of members (n < 11) who had their first SMA claim after their second birthday. 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 and ethnicity.

Our cost model estimated annual cost for the treatment based on the drug indication prevalence estimates and assumptions for treatment uptake, as well as average drug acquisition costs and statutorily required rebates. Refer to Appendix A for additional detail on how we conducted this study.

How Common Was Zolgensma Use Among Medicaid Members in 2019 to 2021?

Zolgensma was approved in May 2019. We identified 146 members with claims for Zolgensma from 2019 through 2021 (excluding Alabama, Illinois, Mississippi, New York, and Utah; Exhibit 4). The number of members who received the treatment increased over time, with 21 members in 2019, 59 members in 2020, and 66 members in 2021. The number of members with Zolgensma claims in 2021 represents 15.9% of the total members we identified as potentially eligible for this treatment.

The average age at treatment for Medicaid members was higher compared to the average age of trial participants. All trial participants were aged less than 8 months, with an average age of 3.7 months, while in the Medicaid cohort the average age at treatment was 7.6 months. While over 41% of the Medicaid members who received this treatment got it within the first 3 months of life, 1 in 3 was older than 8 months of age, which is entirely outside the age range of trial participants.

EXHIBIT 4

Members aged under 2 years with SMA who had Zolgensma claims in Medicaid, 2019 to 2021

	with Zolgensma claims[a]	%[b]
Total members	*459*	-
Age at treatment, in months		
0 to 2	131	28.5
3 to 5	177	38.6
6 to 11	151	32.9
12 to 24		
Sex		
Female	215	47.4
Male	239	53.6
Race and ethnicity		
Hispanic	79	31.2
White, non-Hispanic	122	48.2
All other race or ethnicity, non-Hispanic	16	6.3

Notes. [a] Excludes dually eligible members and all members in Alabama, Illinois, Mississippi, New York, and Utah. [b] Percentage of members with nonmissing data on demographic characteristics. Abbreviation. SMA: spinal muscular atrophy.

What Was the Impact of Zolgensma on State Medicaid Spending for 2019 to 2021?

We estimate that total Medicaid spending on Zolgensma was $276.2 million nationally from May 2019 (when it first became available) through 2021, with $175.1 million of this cost coming from federal funds and the remaining $101.1 million coming from state funds. This estimate is based on converting the total number of Zolgensma claims into a dollar cost using the price of the treatment at the time ($2,125,000 per dose) and applying the statutorily required rebates. Refer to Appendix A for additional detail on how the costs were calculated.

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

Due to provisions of the Omnibus Budget Reconciliation Act of 1990 that 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 approval, is a key factor in establishing the requirement for Medicaid coverage. We estimate that the future total annual cost of Zolgensma for SMA treatment in Medicaid to be $158.9 million (95% confidence bounds, $139.1 million and $288.6 million). This corresponds to a per-member per-month (PMPM) cost of $0.17 (95% confidence bounds, $0.15 and $0.31) for all Medicaid members. Based on the enrollment composition of the members with Zolgensma claims in CHIP (Children's Health Insurance Program) and Medicaid in 2021, and the weighted national average of corresponding fed-

eral match rates, we estimate that $93.5 million of the total annual costs would come from federal funds and the remaining $65.4 million would be paid by the states. This estimate is based on the current price of the treatment, the Medicaid incidence assumption of 1 Medicaid member with type 1 or type 2 SMA per 42,350 births (about 85 new members eligible for Zolgensma each year), and an estimate that the uptake rate will increase by 15% from the 2021 level. Refer to the Methods Appendix (Appendix A) for additional detail on model inputs and assumptions.

CONSIDERATIONS

Zolgensma received FDA approval based on 2 trials including 36 children, demonstrating longer durations of survival to either death or permanent ventilation relative to what would have been expected based on historical controls.[4] While this outcome is clearly important for families, clinicians, and Medicaid administrators, the true efficacy of Zolgensma relative to no treatment has not been established. Further, whether and which concurrent treatments are also needed along with Zolgensma has not been fully established. State Medicaid program staff could consider monitoring health care service use by children who received Zolgensma, including use of other drug therapies, inpatient stays and emergency department visits, to understand patterns of care usage after the one-time treatment.

Medicaid coverage policies vary by state and treatment choice, leading to concerns about uneven access to treatment among children with SMA.[25] In some states, Medicaid coverage guidelines for Zolgensma require prior authorization.[25] The other requirements for coverage include no concurrent use of other available treatments, no previous use of Zolgensma, *SMN2* gene counts, ventilation status, and specialty care services.[25] In some states and Medicaid managed care organizations, Medicaid coverage for Zolgensma is more restrictive than the FDA-approved population because the FDA's eligibility criteria are broader than those used in clinical trials.[26]

While SMA is relatively rare, Zolgensma is a very expensive therapy. We estimated Medicaid spending on Zolgensma to be $276.2 million between May 2019 through 2021. While it received full FDA approval, this approval was based on single arm open-label trials,[4] and long-term outcomes are currently under study.[5] State Medicaid program administrators should continue to monitor for evidence of long-term efficacy to allow for accurate planning of future expenditures related to SMA. Further, state Medicaid program administrators should consider their coverage criteria for Zolgensma, as some states limit coverage of Zolgensma to mirror the population included in the clinical trials, as opposed to the broader FDA approval.

In summary, Zolgensma represents a potentially successful treatment for a fatal genetic disease. However, due to the relatively small studies that led to its approval, the full scope and magnitude of the benefits and harms of Zolgensma are not yet truly known. To inform future management strategies, state Medicaid programs can monitor health care service usage among children who received Zolgensma in their state.

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APPENDIX A

METHODS

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

APPENDIX B

DEMOGRAPIC INFORMATION

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

APPENDIX C

BASELINE CHARACTERISTICS OF TRIAL PARTICIPANTS

See attachment for a table describing the characteristics of the patients with SMA who participated in the studies used to approve Zolgensma.

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