MEDICAID EVIDENCE REVIEW AND COST INITIATIVE BRIEF

Tisotumab Vedotin (Tivdak) for Cervical Cancer

OVERVIEW

In 2021, the US Food and Drug Administration (FDA) gave tisotumab vedotin-tftv (branded as Tivdak) accelerated approval for the treatment of recurrent or metastatic cervical cancer in adults who had disease progression during or after chemotherapy.[1,2] The accelerated approval was based on the surrogate clinical endpoints of tumor response rate and duration of response.[3] In 2024, the drug manufacturer submitted confirmatory trial results requested by the FDA and received traditional drug approval for tisotumab vedotin-tftv.

Cervical cancer has the fourth highest mortality rate among cancers in women,[4] and according to our analysis, nearly 6,000 female Medicaid members aged 18 to 64 years were identified as having recurrent or metastatic cervical cancer in 2021. Treatment options for cervical cancer depend upon the stage of cancer and can include chemotherapy, radiation therapy, and surgery.[5] More recently, therapies targeting specific forms of cervical cancer are available, such as bevacizumab (Avastin), pembrolizumab (Keytruda), and tisotumab vedotin-tftv (Tivdak).[6]

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.

It is estimated that Medicaid will spend approximately $53.9 million total for treatment with tisotumab vedotin-tftv each year (based on cervical cancer prevalence among Medicaid enrollees and drug pricing in 2021), with $37.6 million coming from federal funds and $16.3 million from state funds. Notably, a recent cost-effectiveness analysis demonstrated that tisotumab vedotin-tftv is likely not cost-effective compared with chemotherapy for recurrent or metastatic cervical cancer.[7]

What Is Cervical Cancer?

Cervical cancer, or cancer to the uterine cervix, starts in the cells of the cervix and usually develops slowly into invasive carcinoma over a period of 10 to 12 years; however, in 10% of people this progression can occur in less than 1 year.[4]

Symptoms of cervical cancer include abnormal vaginal bleeding, unusual vaginal discharge, pain during sex, and pain in the lower back and pelvic region.[5,8] In the advanced stages, people with cervical cancer may also experience blood in urine, swelling in the legs, and difficulty urinating or having a bowel movement.[8] Screening for cervical cancer with examination of the cervical cells (i.e, Papanicolaou test [Pap smear]) and human papillomavirus (HPV) tests can help to identify early precancerous changes that may warrant increased monitoring with additional or more frequent tests, or lead to early treatment.[5,8]

CERVICAL CANCER and TISOTUMAB VEDOTIN-TFTV

OVERVIEW

CERVICAL CANCER PREVALENCE

IN THE US

In 2021, an estimated 295,748 women were living with cervical cancer.[11]

IN MEDICAID

Of female Medicaid members aged 18 to 64 years, 20,121 had cervical cancer and 5,944 had recurrent or metastatic cervical cancer in 2021.

TISOTUMAB VEDOTIN-TFTV FACTS

DRUG PRICE PER PATIENT

$466,208 per year

FDA ACCELERATED APPROVAL DATE

September 2021

FDA TRADITIONAL APPROVAL DATE

April 2024

MEDICAID COST ESTIMATES

PROJECTED ANNUAL COST TO MEDICAID

National estimate to treat Medicaid members: $53.9 million, with $37.6 million coming from federal funds and $16.3 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 tisotumab vedotin-tftv.
Abbreviations. FDA: US Food and Drug Administration.

How Many People Have Cervical Cancer?

Cervical cancer is the fourth most common cancer in women worldwide, and it has the fourth highest mortality rate among cancers in women.[4] In the US, about 13,820 new cases of cervical cancer are diagnosed annually, and about 4,360 women die of this cancer every year.[4] Most cervical cancer diagnoses are in people with no or very limited history of screening.[4]

The 5-year relative survival rate for all people with cervical cancer is 67%; however, depending on the stage at diagnosis and the spread of disease, the 5-year survival rate ranges from 19% (when diagnosed after the disease has metastasized to a distant part of the body) to 91% (when diagnosed at an early stage).[9] The rate for new cervical cancer cases is highest in people who identify as Hispanic or non-Hispanic American Indian and Alaska Native (8.4 new cases per 100,000 people), but the mortality rate is highest in people who identify as non-Hispanic Black (3.2 deaths per 100,000 people).[10]

How Is Cervical Cancer Identified and Managed?

Current guidelines recommend screening for cervical cancer every 3 to 5 years, depending on age.[12] Following an abnormal Pap smear, additional diagnostic tests including colposcopy (cervical tissue biopsies) can be performed to gain more information; if the tests are positive for cancer, an individual may undergo further investigation to stage the spread of cancer.[8]

Treatment options for cervical cancer depend upon the stage of cancer and can include chemotherapy, radiation therapy, and surgery.[5] More recently, therapies targeting specific forms of cervical cancer are available, including bevacizumab (Avastin), pembrolizumab (Keytruda), and tisotumab vedotin-tftv (Tivdak).[6]

A number of factors contribute to disparities across the cervical cancer care continuum.[13] In the US, people from racial and ethnic minority groups, people who are socioeconomically disenfranchised, and those in rural areas have lower rates of HPV vaccination, screening, and treatment of cervical cancer, which can lead to worse outcomes.[14] Estimates of the total annual medical cost for cervical and uterine cancer care in the US was $2.3 billion in 2020, and accounted for 1.1% of all cancer treatment costs.[15]

How Much Does Cervical Cancer Cost to Treat?

According to the National Cancer Institute the cost of cervical cancer care in the US was $2.3 billion in 2020.[16] The cost per patient varies over the course of treatment with average costs of $58,700 in the first year of care and $97,000 in the year preceding the end-of-life.[16]

DRUG INFORMATION

In 2021, tisotumab vedotin-tftv was approved through the FDA's accelerated approval pathway for the treatment of recurrent or metastatic cervical cancer in those adults who had disease progression during or after chemotherapy.[1,2] The approval was based on the surrogate clinical endpoints of tumor response rate and duration of response.[3]

TISOTUMAB VEDOTIN-TFTV Tivdak®

DRUG SUMMARY

BASIC INFORMATION

DRUG CLASS
Tissue factor-directed antibody and microtubule inhibitor conjugate

MANUFACTURER
Seagen; Genmab; Pfizer[a]

PRICE PER PATIENT $466,208 per year

FDA APPROVAL

PATHWAY Accelerated approval

DATE September 2021

PRESCRIBING LABEL
https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761208s007lbl.pdf

APPROVED INDICATION(S)

For the treatment of adult patients with recurrent or metastatic cervical cancer who have had disease progression during or after chemotherapy

DOSING

ROUTE Intravenous (IV)

FORMULATION
40 mg as a lyophilized cake or powder in a single-dose vial for reconstitution

INFORMATION
2 mg/kg (up to a maximum of 200 mg), every 3 weeks

Administered as IV infusion over 30 minutes until disease progression or unacceptable toxicity

SAFETY

BOXED WARNINGS
Can cause severe ocular toxicities resulting in changes in vision, including severe vision loss and corneal ulceration. Conduct an ophthalmic exam, including an assessment of ocular symptoms, visual acuity, and slit lamp exam of the anterior segment of the eye prior to initiation of tisotumab vedotin-tftv, prior to every cycle for the first 9 cycles, and as clinically indicated. Adhere to the required premedication and eye care before, during, and after infusion. Withhold until improvement and resume, reduce the dose, or permanently discontinue, based on severity.

PRECAUTIONS
Peripheral neuropathy: monitor patients for new or worsening peripheral neuropathy. Withhold, reduce the dose, or permanently discontinue tisotumab vedotin-tftv based on severity.
Hemorrhage: monitor patients for signs and symptoms of hemorrhage. Withhold, reduce the dose, or permanently discontinue tisotumab vedotin-tftv based on severity.
Pneumonitis: severe, life-threatening or fatal pneumonitis may occur. Withhold tisotumab vedotin-tftv for persistent or recurrent grade 2 pneumonitis and consider dose reduction. Permanently discontinue tisotumab vedotin-tftv for grade 3 or 4 pneumonitis.
Severe cutaneous (skin) adverse reactions: severe cutaneous adverse reactions, including events of fatal or life-threatening SJS, can occur in patients treated with tisotumab vedotin-tftv. Immediately withhold tisotumab vedotin-tftv for suspected severe cutaneous adverse reactions, including SJS. Permanently discontinue tisotumab vedotin-tftv for confirmed grade 3 or 4 severe cutaneous adverse reactions, including SJS.
Embryo-fetal toxicity: tisotumab vedotin-tftv can cause fetal harm. Advise of the potential risk to a fetus and to use effective contraception.

ADVERSE REACTIONS
Decreased hemoglobin, fatigue, decreased lymphocytes, nausea, peripheral neuropathy, hair loss (alopecia), nosebleeds (epistaxis), conjunctival adverse reactions, hemorrhage, decreased leukocytes, increased creatinine, dry eye, increased prothrombin international normalized ratio, activated partial thromboplastin time prolonged, diarrhea, and rash

Notes. Information reflects that of the most recent prescribing label and not that of the original accelerated approval. [a]In 2023, Pfizer acquired Seagen Inc.[27]
Sources. IPD Analytics and the US Food and Drug Administration (FDA).
Abbreviations. FDA: US Food and Drug Administration; SJS: Stevens-Johnson syndrome

FINDINGS

What Evidence Was Used by the FDA to Approve Tisotumab Vedotin?

Exhibit 1 provides a summary of the study used to approve tisotumab vedotin-tftv through the accelerated pathway.

Why Did the FDA Grant Accelerated Approval?

When evaluating tisotumab vedotin-tftv, the FDA considered efficacy results from the innovaTV 204 study. In this trial, 101 participants received at least 1 dose of tisotumab vedotin-tftv every 3 weeks until disease progression continued, or until there was unacceptable toxicity.[3] The confirmed objective response rate was 24% (95% CI, 16% to 33%); complete response rate was 7% and the partial response rate was 17%.[3] In the 24 participants with a response, the median duration of response was 8.3 months.[3] The endpoints used for the accelerated approval of tisotumab vedotin-tftv are generally considered by the FDA as surrogate endpoints (i.e., endpoints that *potentially* predict clinical benefit).[1,20]

The tisotumab vedotin-tftv label has a boxed warning about ocular toxicity, as well as a series of other precautions and adverse reactions.[3] Tisotumab vedotin-tftv may cause changes in the corneal epithelium and conjunctiva resulting in changes in vision, such as severe vision loss and corneal ulceration.[3] Clinical precautions include

EXHIBIT 1

Summary characteristics of the study used to support efficacy of tisotumab vedotin-tftv

	innovaTV 204[18,19]
Official title	A single arm, multicenter, international trial of tisotumab vedotin (HuMax TF-ADC) in previously treated, recurrent or metastatic cervical cancer
ClinicalTrials.gov ID	NCT03438396
Study design	Single-arm, open-label (nonrandomized, unblinded) trial
Clinical trial phase	Phase 2
Study population description	102 adults with extra-pelvic metastatic or recurrent cervical cancer including squamous cell, adenocarcinoma or adenosquamous histology, who have experienced disease progression on standard of care chemotherapy in combination with bevacizumab; 101 participants received at least 1 dose of tisotumab vedotin-tftv
Patient status requirement	Eastern Cooperative Oncology Group Performance Status 0 or 1
Intervention	Tisotumab vedotin-tftv, 2.0 mg/kg (up to a maximum of 200 mg) by IV infusion every 3 weeks, for approximately 20 months
Control	No comparator group
Primary outcome used for accelerated approval	Objective response rate and duration of response
Trial funding	Genmab, Seagen, Gynaecologic Oncology Group, and European Network of Gynaecological Oncological Trial Groups

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. IV: intravenous.

the need to monitor for peripheral neuropathy, hemorrhage, lung inflammation, and severe adverse skin reactions, as well as to advise of the risk of embryo-fetal toxicity.[3] The most common adverse reactions (occurring in at least 25% of people) are decreased hemoglobin, fatigue, decreased lymphocytes, nausea, peripheral neuropathy, hair loss (alopecia), nosebleeds (epistaxis), conjunctival adverse reactions, hemorrhage, decreased leukocytes, increased creatinine, dry eye, blood clotting slower than normal (increased prothrombin international normalized ratio, or activated partial thromboplastin time prolonged), diarrhea, and rash.[3]

What Studies Were Requested to Convert Tisotumab Vedotin to Full Approval?

As part of the accelerated approval in 2021, the FDA requested final overall survival and progression-free survival analyses to describe and verify the clinical benefit of tisotumab vedotin-tftv in people with recurrent or metastatic cervical cancer.[21,22] The original projected trial completion date was May 2024.[21]

In 2024, early findings from the ongoing confirmatory trial were accepted by the FDA, and based on these findings tisotumab vedotin-tftv was converted to traditional approval in April 2024.[23,24]

EXHIBIT 2

Summary characteristics of the study requested to support full approval

	innovaTV 301[21,25]
Official title	A randomized, open-label, phase 3 trial of tisotumab vedotin vs. investigator's choice chemotherapy in second- or third-line recurrent or metastatic cervical cancer
ClinicalTrials.gov ID	NCT04697628
Study design	Randomized, open-label, active-controlled trial
Study population description	568 adults (aged 18 years and older) with recurrent or metastatic cervical cancer with squamous cell, adenocarcinoma, or adenosquamous histology, and disease progression during or after treatment with a standard of care systemic chemotherapy doublet, or platinum-based therapy
Study arms	2 study arms
Intervention	Tisotumab vedotin-tftv, 2.0 mg/kg, administered by IV infusion every 3 weeks
Control	Investigator's choice of 1 chemotherapy treatment (topotecan, vinorelbine, gemcitabine, irinotecan, or pemetrexed)
Study duration	Up to 2 years
Study sites	194 sites located in 26 countries, including the US
Trial funding	Seagen Inc.
Primary outcome	Overall survival
Outcomes requested by the FDA	Overall survival and progression-free survival
Status of requested study	Active, not recruiting
Primary completion date	July 2023 (actual)

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

DATA METHODS SUMMARY

Tisotumab vedotin-tftv is indicated for adult patients with recurrent or metastatic cervical cancer who have disease progression during or after chemotherapy. Researchers at the Center for Evidence-based Policy (Center) used the Centers for Medicare & Medicaid Services (CMS) Transformed Medicaid Statistical Information System (T-MSIS) and associated T-MSIS analytic files to identify Medicaid members with cervical cancer, and those with recurrent or metastatic cervical cancer who had previously received chemotherapy.

Specifically, we first identified adult female members ages 18 to 64 with at least 1 inpatient or 2 outpatient claims with a cervical cancer diagnosis [ICD-10 C53]. To identify recurrent or metastatic patients, we used a previously validated algorithm based on systematic treatments, not concomitant with surgery or radiation therapy, relying on procedure codes and National Drug Code (NDC) reported in inpatient, outpatient, and pharmacy claims.[26] 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, Alabama and Utah 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 generally did not report data elements for states identified as '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 recurrent and metastatic cervical cancer.

Cervical cancer analysis cohorts were anchored in 2021, with a 3-year lookback period to ensure comprehensive Medicaid member identification. Health care service use and comorbidities among cervical cancer patients was compared to the Medicaid-insured population at-large using a 3-to-1 exact matching method based on state, age (in years), sex, and race and ethnicity. Our service usage metrics do not have a continuous enrollment requirement.

Our cost model estimated annual cost for the drug using inputs of drug indication prevalence, drug uptake, and average treatment duration observed in the 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.

Why Did the FDA Grant Full Approval?

Primary endpoint results (namely, overall survival) of the innovaTV 301 trial were used to approve tisotumab vedotin-tftv through the traditional pathway.[24] The FDA considers overall survival a clinical endpoint that can be employed by industry for the traditional approval of cancer drugs.[20] Exhibit 2 provides a summary of the study used for traditional approval.

Tisotumab vedotin-tftv was associated with significantly improved overall survival compared with chemotherapy (48.6% of people receiving tisotumab vedotin-tftv died, vs. 56.2% of people receiving chemotherapy).[3] People in the tisotumab vedotin-tftv group also had significantly improved progression-free survival and a significantly higher response to treatment than people in the chemotherapy group.[3]

How Common Is Cervical Cancer Among Medicaid Members?

Our analytic cohort included 26,203,161 non-dually eligible female Medicaid members aged 18 to 64 in 2021. Of these, 20,121 (or 7.7 per 10,000 female members aged 18 to 64 years) were identified as having cervical cancer and 5,944 (or 2.3 per 10,000 female members aged 18 to 64 years) as having recurrent or metastatic cervical cancer.

Among Medicaid enrollees identified with cervical cancer, 51.9% identified as non-Hispanic White, 25.4% as Hispanic, and 16.3% as non-Hispanic Black (Exhibit 3). Nearly two-thirds (58%) of cervical cancer patients were over the age of 45, and only 12.7% were under the age of 35. The demographic composition of recurrent and metastatic cervical cancer patients was similar.

The prevalence of cervical cancer among state Medicaid populations varied somewhat among the states for which there was available data, from 3.4 cases per 10,000 female members aged 18 to 64 years in Vermont, to over 13 cases per 10,000 of these members in Wyoming. Cervical cancer prevalence also topped 10 cases per 10,000 female members aged 18 to 64 years in Florida, Missouri, Ohio, and Texas (Exhibit 4). This pattern was largely similar for the prevalence of recurrent or metastatic cervical cancer (see Appendix C for state prevalence).

How Do Medicaid Members With Cervical Cancer Compare With Tisotumab Vedotin Trial Populations?

The racial and ethnic demographic characteristics of patients included in the drug trial varied substantially from our Medicaid cohort in terms of composition. While both the study and Medicaid

EXHIBIT 3

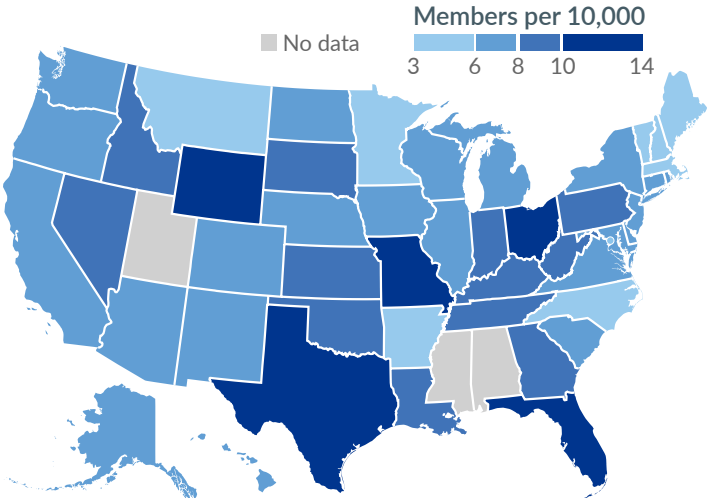
Characteristics of female Medicaid members aged 18 to 64 years with and without cervical cancer, 2021

	with recurrent or metastatic cervical cancer[a,b]	%[c]	with any cervical cancer[a]	%[c]	without cervical cancer[a]	%[c]
Total members	*5,944*	-	*20,121*	-	*26,183,040*	-
Age, in years						
18 to 34	665	11.2	2,565	12.7	13,698,414	52.3
35 to 44	1,675	28.2	5,962	29.6	5,751,354	22.0
45 to 54	1,776	29.9	5,802	28.8	3,595,597	13.7
55 to 64	1,828	30.8	5,792	28.8	3,137,675	12.0
Race and ethnicity						
American Indian or Alaska Native, non-Hispanic	87	1.9	196	1.4	280,227	1.5
Asian, non-Hispanic	185	4.1	577	4.0	861,559	4.7
Black, non-Hispanic	732	16.1	2,351	16.3	3,765,770	20.4
Hispanic	1,100	24.1	3,664	25.4	5,236,170	28.4
Native Hawaiian or Pacific Islander, non-Hispanic	-[d]	-[d]	59	< 1	90,719	< 1
White, non-Hispanic	2,392	52.5	7,486	51.9	8,014,845	43.5
Multiracial, non-Hispanic	-[d]	-[d]	68	< 1	135,108	< 1
Other race or ethnicity	-[d]	-[d]	28	< 1	50,620	< 1

Notes. [a] Excludes dually eligible members and members in Alabama, Mississippi, and Utah. [b] Excludes members in Illinois and New York due to data quality issues for procedure codes. [c] Percentage of members with nonmissing data on demographic characteristics; 14,429 (71.7%) of members with cervical cancer and 18,435,018 (70.4%) of members without cervical cancer had nonmissing race/ethnicity data. For more detail see Appendix B. [d] Suppressed (at least 1 group N < 11).

EXHIBIT 4

Cervical cancer prevalence in Medicaid per 10,000 female members aged 18 to 64 years, by state, 2021



Note. Data not available for Alabama, Mississippi, and Utah.

EXHIBIT 5

Prevalence of affected body systems in female Medicaid members aged 18 to 64 years with and without cervical cancer, 2021

	Medicaid members with cervical cancer		Matched Medicaid members without metastatic lung cancer	
System or condition	N	%[a]	N	%[a]
Total members[a]	*19,845*	-	*59,535*	-
Cardiovascular	8,230	41.5	15,579	26.2
Gastrointestinal	5,560	28.0	7,255	12.0
Infectious disease	3,228	16.3	2,391	4.0
Metabolic	3,770	19.0	2,649	4.4
Psychological	5,024	25.3	11,139	18.7
Pulmonary	4,078	20.5	6,812	11.4
Renal	4,641	23.4	3,088	5.2
Skeletal	3,272	16.5	7,710	13.0

Note. [a] Members included in this calculation are those with at least 1 inpatient or 1 outpatient claim in 2021. There were 206 members with metastatic cervical cancer who did not have any Medicaid claims in 2021 and were eliminated from this calculation along with their matched comparisons.

cohorts were primarily White, the tisotumab vedotin-tftv study cohort was much more predominantly so (95% White in the trial compared with 51.9% non-Hispanic White in Medicaid). Only 6% of the study cohort were Hispanic and 1% Black or African American, compared with 25.4% Hispanic and 16.3% non-Hispanic Black in the Medicaid cohort. The trial and Medicaid population were similar in terms of age, with a mean age of 50 years in the trial cohort and 47 years in the Medicaid cohort.

Exhibit 5 describes the prevalence of the most common body system-level impairments for Medicaid members aged 18 to 64 years with cervical cancer, and compares with members without any cervical cancer (matched 1:3 on state, age, sex, and race and ethnicity) identified in 2021 Medicaid claims using the Chronic Disability Payment System methodology. A larger proportion of members with cervical cancer had comorbid conditions across all body systems than their matched comparisons. Cardiovascular conditions were most common among both groups; 41.2% of members with cervical cancer were affected by this condition compared with 26.2% of their matched comparisons. Other commonly affected body systems for members with cervical cancer included gastrointestinal, psychological, and renal conditions.

Members with cervical cancer had higher hospital and emergency use than their matched counterparts (Exhibit 6). Specifically, 33.3% of Medicaid members with cervical cancer experienced at least 1 hospitalization in 2021, compared with 9.6% of matched members without cervical cancer. Members with cervical cancer also experienced more total inpatient days (8,082 vs. 1,303 per 1,000 members), were more likely to experience hospital stays lasting at least 5 days (18.1% vs. 3.8%), and had higher emergency department use across multiple measures.

EXHIBIT 6

Health service use by matched female Medicaid members aged 18 to 64 years with and without cervical cancer, 2021

	Members with cervical cancer[a]	Matched members without cervical cancer[a]
Total members	*20,121*	*60,363*
Hospitalizations		
% with ≥ 1 hospitalization	33.3	9.6
% with ≥ 2 hospitalizations	16.9	2.5
Total hospitalizations, per 1,000 members	757	144
Total inpatient days, per 1,000 members	8,082	1,303
Average length of stay per hospitalization, days	10.7	9.0
% with ≥ 1 hospitalization lasting ≥ 5 days	18.1	3.8
Emergency department (ED) visits		
% with ≥ 1 ED visit	54.3	31.2
% with ≥ 5 ED visits	11.6	3.0
Total ED visits per 1,000 members	1,810	719

Note. [a] Medicaid members without cervical cancer matched to members with cervical cancer at 3:1 on state of residence, age, sex, race, and ethnicity.

What Is the Potential Impact of Tisotumab Vedotin on State Medicaid Spending?

We estimated that the total annual cost of tisotumab vedotin-tftv for recurrent and metastatic cervical cancer treatment in Medicaid would be $54 million nationally (95% confidence bounds, $12.3 million and $158.6 million), based on cervical cancer prevalence among Medicaid enrollees and drug uptake and pricing in 2021. This corresponds to a per-member per-month cost of $0.06 (95% confidence bounds, $0.01 and $0.17) for all Medicaid members. Based on the enrollment composition of the cervical cancer patients in CHIP (Children's Health Insurance Program) and Medicaid expansion, and the weighted national average of corresponding federal match rates, we estimated that $37.6 million of the total cost would come from federal funds and the remaining $16.3 million would be paid for by the states each year. The number of patients eligible for the treatment is based on the recurrent or metastatic cervical cancer prevalence observed in 2021 Medicaid data. The uptake rate and other inputs used in cost calculations are based on inputs from the literature and other sources. Refer to the Methods Appendix (Appendix A) for additional detail on model inputs and assumptions.

Comparing these estimates against Medicaid total 2022 spending estimates reported elsewhere,[27] tisotumab vedotin-tftv would potentially account for 0.12% of the total Medicaid prescription drug spending.

Exhibit 7 shows the total projected cost estimates for different uptake and average treatment duration scenarios. At the highest uptake rate and average treatment duration (40% and 6 months, respectively), the estimated total annual cost of tisotumab vedotin-tftv is more than $185 million. At the lowest rates of uptake rate and average treatment duration (5% and 1 month, respectively), the estimated total annual cost is about $4 million.

EXHIBIT 7

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

Average treatment duration (months)	Uptake (share of eligible Medicaid members)							
	5%	10%	15%	**20%**	25%	30%	35%	40%
1	4	8	12	15	19	23	27	31
2	8	15	23	31	39	46	54	62
3	12	23	35	46	58	69	81	93
3.5	13	27	40	**54**	67	81	94	108
4	15	31	46	62	77	93	108	123
5	19	39	58	77	96	116	135	154
6	23	46	69	93	116	139	162	185

Considerations

Tisotumab vedotin-tftv is an example of an accelerated approval that aligns with the FDA's intended use of the pathway, namely to allow for earlier approval of drugs that treat a serious condition and fill an unmet medical need as demonstrated by a surrogate endpoint, followed-up by timely completion of the requested clinical trial to confirm the anticipated benefit.[28] Tisotumab vedotin-tftv first received FDA accelerated approved in September 2021, with traditional approval following in April 2024 based on confirmatory trial results demonstrating improved overall survival compared with chemotherapy, and higher response to treatment than in the chemotherapy group.[3] With traditional approval in place, state and federal policymakers should plan for total tisotumab vedotin-tftv expenditures of around $54 million annually, with $37.6 million of the total costs coming from federal funds and the remaining $16.3 million coming from state funds.

It is important to reiterate that the demographics of the study population for tisotumab vedotin-tftv varied substantially from our Medicaid cohort in terms of racial and ethnic composition. While both the study and Medicaid cohorts were primarily White, the tisotumab vedotin-tftv study cohort was much more predominantly so; only 6% of study cohort were Hispanic and 1% Black or African American, compared with 25.4% Hispanic and 16.3% non-Hispanic Black in the Medicaid cohort. As a result, patients, clinicians, and state and federal policymakers should continue to monitor for treatment results and adverse reactions in Hispanic and Black or African American Medicaid members receiving this therapy.

There is, however, more that patients, their clinicians, and state and federal policy makers should consider about treatment with tisotumab vedotin-tftv. Compared with chemotherapy, tisotumab vedotin-tftv may to increase survival by 2 months (11.5 months vs. 9.5 months),[24] but patients should be informed of severe risks, including a vision-loss boxed warning, when considering this therapy.[3] In addition, a recent analysis demonstrates that the high cost of

tisotumab vedotin-tftv means it is not cost-effective compared with chemotherapy for recurrent or metastatic cervical cancer.[7] The high cost and the serious risk of vision loss may prompt patients and their clinicians, and state and federal policymakers to consider other therapies.

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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 inputs for recurrent or metastatic cervical cancer patients

APPENDIX B

DEMOGRAPHIC INFORMATION

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

APPENDIX C

MEDICAID MEMBERS WITH AND WITHOUT CERVICAL CANCER, 2021

See attachment for this table.

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