MILLIMAN WHITE PAPER

Demographic Characteristics of Accelerated Approval Drug Utilizers in Medicaid

Commissioned by PhRMA

Katie Holcomb, FSA, MAAA
Briana Botros, FSA, MAAA
Kristin Niakan, MPH
Benton Whaley

Milliman

SUMMARY

The US Food and Drug Administration's (FDA) accelerated approval pathway enables expedited access to drugs that address an unmet need for serious and life-threatening diseases and conditions. Milliman analyzed the demographic characteristics of Medicaid beneficiaries who utilize accelerated approval drugs using 2018-2019 national data from the Transformed Medicaid Statistical Information System (T-MSIS). Overall, we found:

- On average, accelerated approval drug utilizers are more likely to be older and are more commonly eligible for Medicaid based on their disability status compared to Medicaid beneficiaries using non-accelerated approval drugs. This is likely related to the types of conditions accelerated approval drugs treat. It is important to note, that some of these drugs may only be indicated for adults, while Medicaid covers a large number of children.
- We observed a higher proportion of Black and Asian beneficiaries using accelerated approval drugs than for all other drug utilizers, based on race and ethnicity data reported in T-MSIS. Demographic characteristics of accelerated approval drug utilizers are directly influenced by the demographic characteristics of populations disproportionately impacted by certain diseases.

BACKGROUND

Accelerated approval allows for the approval of drugs that treat serious or life-threatening diseases conditions and that fill an unmet medical need based upon measure of a surrogate endpoint[1]. A surrogate endpoint is a marker, such as a laboratory result or imaging, that is reasonably likely to predict a clinical benefit, but is not a measure of how the patient feels, functions or survives.[2] Surrogate endpoints facilitate earlier access than a traditional approval because they can be measured earlier than a direct measure of clinical benefit, such as overall survival. This is beneficial especially when direct measures of clinical benefit require long study periods. Following accelerated approval, manufacturers are required to conduct post-approval studies to verify the anticipated clinical benefit. Upon verification of a clinical benefit, the drug can be converted to traditional approval. However, the accelerated approval can be withdrawn if post-approval studies fail to verify the expected clinical benefit.

The accelerated approval pathway was formally established by the FDA in 1992 in recognition of the urgent unmet medical need for treatments with lifesaving potential during the HIV / AIDS epidemic.[3] Between the program's initiation in 1992 and 2010, accelerated approval was predominantly utilized for drugs to treat HIV, cancer, and rare conditions. From 2010 to 2020, 85% of drugs approved via accelerated approval were oncology drugs.[4] Figure 1 below illustrates the therapeutic classes that have had drugs with accelerated approval in recent years.

Figure 1. Number of accelerated approval drugs approved in 2018 through 2021 by therapeutic class.

Therapeutic Class	2018	2019	2020	2021
Antineoplastics	14	9	28	17
Muscular Dystrophy Agents	0	1	1	1
Immunomodulators	0	0	0	1
Antibiotics	1	1	2	0
Sickle Cell Disease	0	1	0	2
Antidotes	0	0	1	0
Metabolic Modifiers	1	0	0	0
Antidementia Agents	0	0	0	1
Natriuretic Peptides	0	0	0	1
Total	**16**	**12**	**32**	**23**

Milliman analysis of CDER Drug and Biologic Accelerated Approvals Based on Surrogate Endpoint as of December 31, 2021 available on the FDA's website.[5]

Drugs approved under accelerated approval made up 28.0% of all FDA drug approvals in 2021 and 22.6% of all FDA drug

[1] https://www.fda.gov/drugs/nda-and-bla-approvals/accelerated-approval-program

[2] https://www.fda.gov/drugs/development-resources/surrogate-endpoint-resources-drug-and-biologic-development

[3] https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/accelerated-approval

[4] https://rarediseases.org/wp-content/uploads/2021/06/NRD-2182-Policy-Report_Accelerated-Approval_FNL.pdf

[5] https://www.fda.gov/media/151146/download

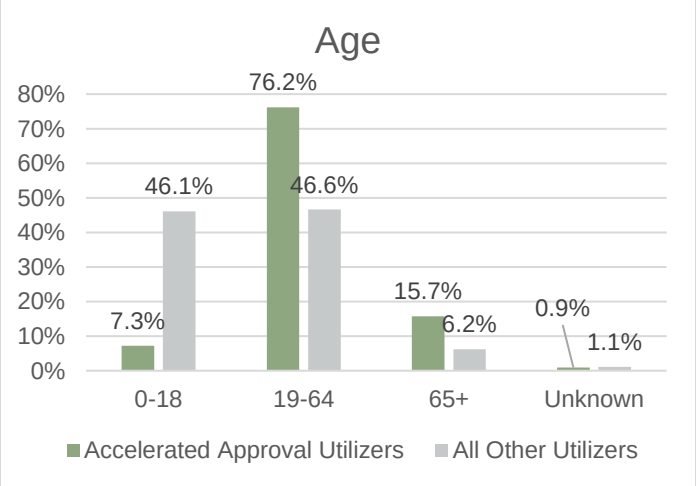
approvals in 2020.[6,7] This is up from 2019 (18.8%), 2018 (6.8%) and 2017 (13.0%).[8,9,10] The overall number of drug approvals dropped in 2020 due to the COVID-19 pandemic, but it is difficult to say whether accelerated approvals were affected similarly as traditional approvals.

RESULTS

The graphs below summarize the 2018 and 2019 demographics of nationwide Medicaid beneficiaries who use accelerated approval drugs compared to the demographics of Medicaid beneficiaries using any other prescription drug, including drugs provided under the medical benefit. Our analysis included 67 million drug utilizers, of which 455,000 were accelerated approval drug utilizers. The demographics summarized include age, sex, income as a percent of the Federal Poverty Level (FPL), race / ethnicity, and disability status (defined by enrollment in Medicaid on the basis of disability). These results include utilization across all indications of drugs ever receiving accelerated approval.

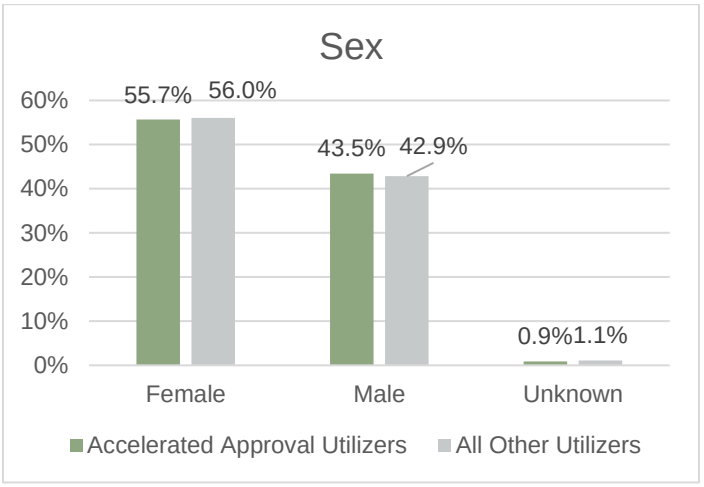
Oncology drugs are some of the most utilized accelerated approval drugs in Medicaid. As such, the demographic characteristics of accelerated approval utilizers is likely reflective of the demographic characteristics of individuals with cancer, which is supported by our results.

Figure 2. Age distribution of accelerated approval drug utilizers compared to all other drug utilizers.



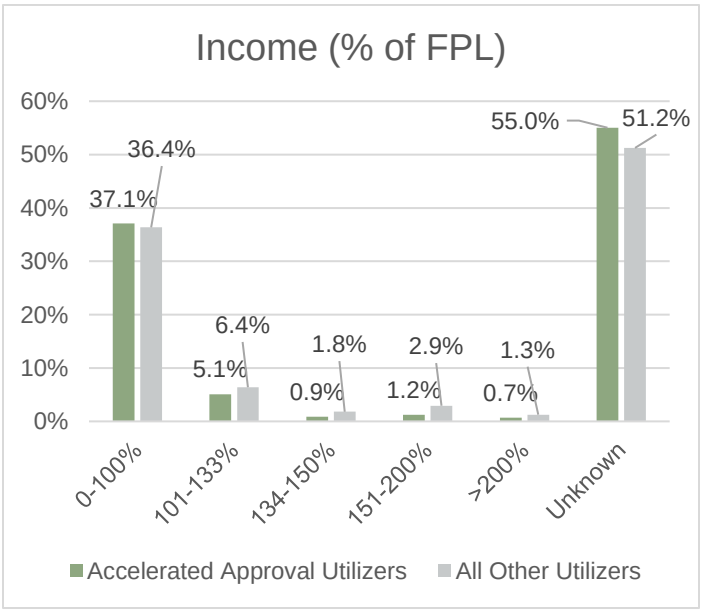
Note, for ages 65 and older, there is lower overall drug utilization than other ages because the majority of utilizers have dual eligibility for Medicare and Medicaid, therefore, a large portion of their drug benefit is covered by Medicare Part D.

Figure 3. Sex distribution of accelerated approval drug utilizers compared to all other drug utilizers.



Note, Medicaid tends to have more female enrollment due to eligibility pathways, such as pathways for pregnant women who are eligible at higher income levels than non-pregnant people and caretakers, who are more likely to be female.

Figure 4. Income distribution of accelerated approval drug utilizers compared to all other drug utilizers.



Note, Medicaid is a program for low-income populations, with limited coverage beyond the FPL.

6 https://www.fda.gov/media/144982/download
7 https://www.fda.gov/media/155227/download
8 https://www.fda.gov/media/134493/download
9 https://www.fda.gov/media/120357/download
10 https://www.fda.gov/media/110526/download

Figure 5. Race and ethnicity distribution of accelerated approval drug utilizers compared to all other drug utilizers.

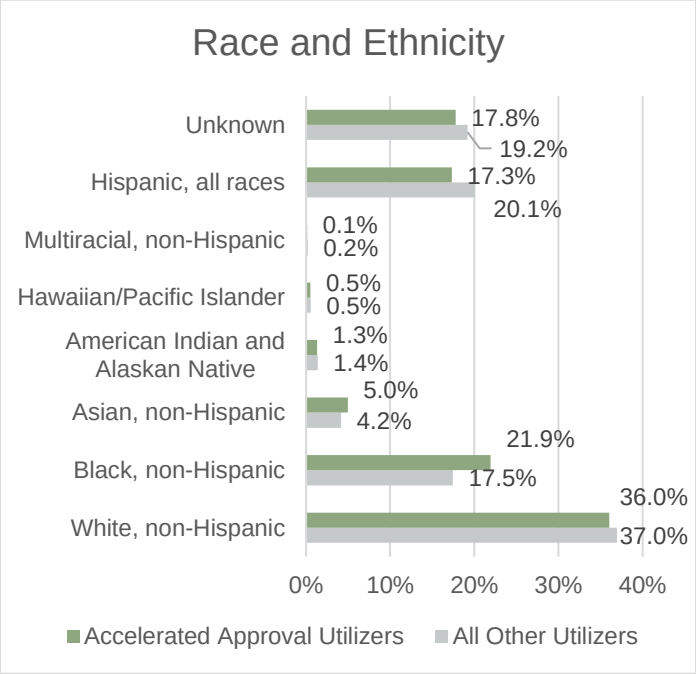
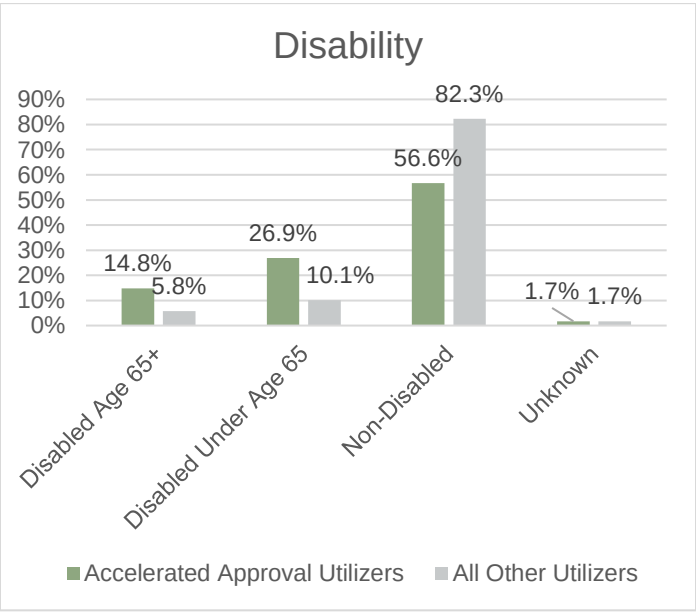


Figure 6. Disability status distribution of accelerated approval drug utilizers compared to all other drug utilizers.



Note, Disability status is defined based on the Medicaid eligibility pathway.

There is a higher proportion of females using drugs for both the population utilizing accelerated approval drugs and the population utilizing other drugs. This is expected, as the proportion of women enrolled in Medicaid is higher in general.

While the sex distribution of members who utilized accelerated approval drugs is very similar to those who did not use accelerated approval drugs, the age distribution is quite different. Accelerated approval drug utilizers skew toward higher age buckets on average and are more likely to be older than members who have not utilized accelerated approval drugs.

The income distribution of patients taking accelerated approval drugs is similar to those who have not taken accelerated approval drugs, although approximately 50% of the sample was excluded due to unknown income level.

The race and ethnicity distributions of patients taking accelerated approval drugs are also fairly similar to those taking non-accelerated approval drugs. The largest amount of beneficiaries taking any type of drug were white, which aligns with the overall racial breakdown of Medicaid enrollees.[11] However, we found that approximately 100,000 (or 22%) of Medicaid beneficiaries who took accelerated approval drugs were Black, compared to 17% of all other drug utilizers. In contrast, we identified approximately 79,000 (or 17%) Medicaid beneficiaries who took accelerated approval drugs were Hispanic, compared to 20% of other prescription drug utilizers.

Demographic characteristics of accelerated approval drug utilizers are directly influenced by the demographic characteristics of populations disproportionately impacted by certain diseases. The demographic characteristics of accelerated approval utilizers is likely reflective of the demographic characteristics of individuals with cancer, which is discussed further later in this report.

The proportion of accelerated approval drug utilizers is higher for those who enrolled in Medicaid through an eligibility pathway for disability at any age compared to those using other drugs. 190,000 of Medicaid accelerated approval drug utilizers are enrolled because of a disability, which constitutes 42% of accelerated approval utilizers, compared to only 16% of all other drug utilizers.

Note, results are limited to utilizers for which demographic data is available. The proportion of utilizers with missing demographic information are displayed in Figures 2 through 6 as “Unknown.” Age, sex, and disability status were populated for nearly 100% of utilizers. Income, on the other hand, was not populated for approximately 50% of utilizers, and this tends to be a field where state system updates may lag. Race / ethnicity was populated for about 80% (for both accelerated approval drug utilizers and utilizers of other prescription drugs).

[11] https://www.kff.org/medicaid/state-indicator/medicaid-distribution-nonelderly-by-raceethnicity/?currentTimeframe=1&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D

DISCUSSION

Oncology drugs are some of the most utilized accelerated approval drugs in Medicaid, according to 2018 and 2019 State Drug Utilization Data[12] (SDUD) claim volume. As such, the demographic characteristics of accelerated approval utilizers is likely reflective of the demographic characteristics of individuals with cancer. Medicaid beneficiaries who are diagnosed with cancer may be more likely to have certain demographic characteristics than other Medicaid beneficiaries, because of the nature of the disease prevalence. For example, white and Black people have the highest incidence of any type of cancer, although American Indian and Alaska Native (AIAN) people have the highest rates of liver and intrahepatic bile duct cancers.[13] It should be noted that the demographic mix in this analysis is reflective of all Medicaid beneficiaries with drug utilization, though the degree of healthcare use (and therefore drug utilization) and rate of diagnosis may vary by demographic group.

In regards to age distribution, the incidence of most cancers increase with age—as such, we would expect accelerated approval utilization to be concentrated in older populations.[14] This aligns with the results of this analysis, which show that the accelerated approval utilization is concentrated in utilizers older than 18. Additionally, research suggests people with disabilities are more likely to develop cancer than compared to people without disabilities. Part of this disparity is due to the mobility and activity limitations of people with disabilities which can contribute to higher incidence of certain cancers such as ovarian cancer, prostate cancer, colorectal cancer, and non-Hodgkin's lymphoma.[15]

Additionally, different types of cancer have different incidence rates depending on sex. According to a KFF study from 2018, overall cancer incidence rates were higher for men than women among white, Black, Hispanic, and AIAN populations, while they were higher for women among Asian and Pacific Islander populations.[16] Our analysis does not show a significantly different sex distribution between accelerated approval utilizers and other prescription drug utilizers; further analysis would be needed to examine the differences among specific cancer types, given some cancers impact females more than males and vice versa.

Other diseases with accelerated approval treatments may impact certain populations disproportionately as well:

- Several Muscular Dystrophy drugs received accelerated approval for treatment in patients who have a confirmed mutation of the Duchenne Muscular Dystrophy (DMD) gene. Research shows white males at younger ages have higher incidence of Muscular Dystrophy.[17] We observed consistent results, with accelerated approval utilization for DMD drugs concentrated in males younger than 18.

- A new treatment for sickle cell disease received FDA accelerated approval in 2019. According to the Centers for Disease Control and Prevention (CDC), sickle cell disease affects both males and females, but is more prevalent in the Black population.[18]

- Conversely, multidrug-resistant tuberculosis more frequently affects Asian, Hispanic, and Black populations. Additionally, the CDC indicates further disparities in prevalence due to homelessness,[19] which would impact populations with lower income levels. These independent reports from the CDC align with our study; we observed accelerated approval utilization for these drugs is concentrated in the group with income below the FPL and Asian utilizers.

- As additional drugs receive FDA accelerated approval for the treatment of Alzheimer's, a disease more prevalent in older populations, results will be further impacted by demographic characteristics of those with Alzheimer's.[20] Alzheimer's drugs did not impact the results in this analysis, as our data was limited to the 2018 and 2019 T-MSIS data, which is prior to the accelerated approval dates for these drugs.

DATA QUALITY OF T-MSIS DEMOGRAPHIC INFORMATION

We relied on 2018-2019 T-MSIS Analytic Files (TAF) Research Identifiable Files (RIFs) for this analysis. CMS hosts an interactive public website containing data quality information for the TAF through the Data Quality Atlas (DQ Atlas).[21] Although states are expected to report information on each field, data quality concerns arise where some states submit incomplete information because the data was not collected or technical difficulties arose in reporting.

The following outlines quality assessment information from the DQ Atlas related to variables used for reporting results of this analysis:

- All states were assigned a "low concern" data quality assessment for both age and sex in 2018 and 2019, meaning all states had 10% or fewer records with missing age and sex information.

- Across both years, 24 states had income data that was missing from more than 50% of records. Income data quality appears to be improving each year.

12 https://www.medicaid.gov/medicaid/prescription-drugs/state-drug-utilization-data/index.html

13 https://www.kff.org/racial-equity-and-health-policy/issue-brief/racial-disparities-in-cancer-outcomes-screening-and-treatment/#:~:text=White%20people%20had%20the%20highest,Pacific%20Islander%2C%20and%20AIAN%20people.

14 https://www.cancer.gov/about-cancer/causes-prevention/risk/age#:~:text=Age%20and%20Cancer%20Risk&text=The%20incidence%20rates%20for%20cancer,groups%2060%20years%20and%20older

15 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9367955/#:~:text=Disparities%20are%20not%20limited%20to,to%20experience%20cancer%20%5B13%5D

16 https://www.kff.org/racial-equity-and-health-policy/issue-brief/racial-disparities-in-cancer-outcomes-screening-and-treatment/#:~:text=White%20people%20had%20the%20highest,Pacific%20Islander%2C%20and%20AIAN%20people

17 https://pubmed.ncbi.nlm.nih.gov/29698937/#:~:text=It%20appears%20that%20DMD%20is,in%20males%20of%20other%20races

18 https://www.cdc.gov/ncbddd/sicklecell/data.html#:~:text=SCD%20occurs%20among%20about%201,sickle%20cell%20trait%20(SCT)

19 https://www.cdc.gov/tb/topic/populations/healthdisparities/default.htm

20 https://www.alz.org/media/documents/alzheimers-facts-and-figures.pdf

21 https://www.medicaid.gov/dq-atlas/welcome

- A meaningful portion of race and ethnicity records was missing in 22 states. There is variability in the quality of race and ethnicity metrics between 2018 and 2019.
- Eligibility codes, which we used to identify utilizers with disabilities, were generally well populated with only six states missing data from 10% to 20% of records.

It should be noted, that the demographic mix in this analysis could be skewed to the extent that the demographic mix of states with a larger proportion of missing data differs from the states with populated data. However, we would expect similar relationships between accelerated approval and other prescription drugs utilization patterns.

One of the challenges in accurately reporting race and ethnicity data is the reliance on self-identification by Medicaid enrollees. Additionally, state Medicaid agencies may face challenges reporting this data, as well including incomplete or inconsistent data collection processes, variations in state reporting practices, and data entry errors.[22]

We compared our observations from the T-MSIS data to other known benchmarks for Medicaid age, sex, race, income distribution, and Medicaid enrollment by eligibility. One important distinction between these benchmarks and our analysis is that public benchmarks generally include all Medicaid enrollees, while our analysis was limited to members who utilized drugs under either the medical or pharmacy benefit. Some groups may have more or less drug utilization than others, such that we would not expect our results to reconcile exactly.

We compared the T-MSIS claim volume for accelerated approval drugs to the claim volume in the SDUD, as well as the Medicaid drug dashboard.[23] Our analysis indicates that T-MSIS data has more claims for many of the accelerated approval drugs compared to SDUD and the Medicaid drug dashboard. This may be due in part to SDUD and Medicaid drug dashboard having redacted claims to comply with the Health Insurance Portability and Accountability Act, as well as the exclusion of 340B drugs. While our total claim counts differ, accelerated approval utilization accounts for a very similar proportion of claims across all sources.

METHODOLOGY

ACCELERATED APPROVAL DRUG LIST

To develop the results of this analysis, we identified drugs approved under the accelerated approval pathway using the CDER Drug and Biologic Accelerated Approvals Based on Surrogate Endpoint as of December 31, 2021 available on the FDA's website.[24] We mapped the drug name to national drug code (NDC) using MediSpan.

We pulled utilization for drugs that ever received FDA accelerated approval. We also sensitivity tested results using a narrower definition in which we mapped the accelerated approval indication for these products to clinically appropriate ICD-10 diagnosis codes in order to capture utilization only for patients with a corresponding diagnosis. If a patient had a corresponding diagnosis at any point between 2016 and 2019, we included that member in the analysis for the narrow definition of accelerated approval. This narrower definition captured a much smaller portion of data, but results were similar for most demographic categories.

DATA SOURCES AND EXCLUSIONS

We relied on the following 2018-2019 national data from the Transformed Medicaid Statistical Information System (T-MSIS) Analytic Files (TAF) Research Identifiable Files (RIF):

- Annual Demographic and Eligibility Files.
- Monthly Claims Files (header and detail records for inpatient hospital services, long-term care services, other services, and pharmacy claims).

We relied on the T-MSIS Annual Demographic and Eligibility File to report on the following demographic characteristics fields:

- Age
- Sex
- Income level relative to the FPL
- Race and ethnicity
- Eligibility Group Code

We relied on the Eligibility Group Code to report on disability status, including Eligibility Group Codes 11 through 26, 37, 39 through 46, 50 through 52, 59, and 60 in our disabled group.

These files include data from both Medicaid managed care and fee-for-service.

We linked the Annual Demographic and Eligibility File to the claims files using beneficiary ID in order to summarize utilization of accelerated drug utilizers and all Medicaid drug utilization by demographic characteristics.

Each pharmacy claim was defined by a unique claim ID and the dollar amount associated with that claim ID. We counted a pharmacy claim as a script if the paid field was non-negative. We excluded claims with a missing beneficiary ID, as the claims data could not be linked to the member-level demographic or diagnosis information without this field. 1.4% of claims were excluded due to a missing beneficiary ID. We focused our review of the 50 states and Washington, D.C., which excluded 1.9% of claims from U.S. territories or claims with a missing or invalid location for the submitting state.

Non-pharmacy medical claims were used to identify beneficiary diagnosis because pharmacy benefit data does not include diagnosis codes.

[22] https://www.kff.org/medicaid/issue-brief/medicaid-administrative-data-challenges-with-race-ethnicity-and-other-demographic-variables/

[23] https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicaid-spending-by-drug

[24] https://www.fda.gov/media/151146/download

CAVEATS AND LIMITATIONS

This report has been prepared for PhRMA. This report is designed to assist PhRMA in better understanding the demographic characteristics of Medicaid recipients who utilize drugs approved under the FDA accelerated approval pathway. Results from this analysis may not be applicable to other third parties. The results presented herein are estimates based on the best information available as of the date of the publication. Differences between our results and other analyses may arise due to variations in definitions, methodology, or data updates.

The results of this analysis are technical in nature and are dependent upon specific assumptions and methods. No party should rely on these results without a thorough understanding of those assumptions and methods. Such an understanding may require consultation with qualified professionals.

Milliman has developed certain models to estimate the values included in this report. The intent of the models was to analyze the demographic characteristics of Medicaid recipients who utilize drugs approved under the FDA accelerated approval pathway. We have reviewed the models, including their inputs, calculations, and outputs for consistency, reasonableness, and appropriateness to the intended purpose and in compliance with generally accepted actuarial practice and relevant actuarial standards of practice (ASOP). The models rely on data and information as input to the models. In preparing this analysis, we relied on various data sources including T-MSIS Analytic Files, State Drug Utilization Data and Eligibility files from Medicaid.gov, CDER Drug and Biologic Accelerated Approval Drug list,[25] Medicaid and CHIP Payment and Access Commission (MACPAC),[26] Kaiser Family Foundation (KFF),[27] and Medi-Span, to develop the results and discussions presented in this report. While we reviewed this data for reasonableness, we did not audit or independently verify any of the information furnished. To the extent that the data and information relied upon is not accurate, or is not complete, the values provided in this report may likewise be inaccurate or incomplete.

Katie Holcomb and Briana Botros are members of the American Academy of Actuaries and meet the qualification standards of the American Academy of Actuaries to perform the analysis supporting this report.

Milliman

CONTACT

Katie Holcomb
katie.holcomb@milliman.com

Briana Botros
briana.botros@milliman.com

Kristin Niakan
kristin.niakan@milliman.com

Benton Whaley
benton.whaley@milliman.com

[25] https://www.fda.gov/drugs/nda-and-bla-approvals/accelerated-approvals

[26] https://www.macpac.gov/

[27] https://www.kff.org/