The Future Cost of Innovation: An Analysis of the Impact of Breakthrough Therapies on Government Spending

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Avalere®

EXECUTIVE SUMMARY

Spending on pharmaceuticals grew 13.1 percent in 2014, with nearly half of this growth driven by new products launched in the last two years, primarily specialty therapies.[1] While medications accounted for approximately 13 percent of healthcare spending in 2013, year-over-year drug trend between 2013 and 2014 was at its highest level since 2001.[2] These spending trends raise questions for government programs and other payers who must balance the potential long-term budget impact of new medications with improvement in patient care.

To evaluate the potential impact of new medications in the drug development pipeline, Avalere projected the fiscal impact of 10 pipeline drugs, designated by the Food and Drug Administration (FDA) as being breakthroughs, to Medicare, Medicaid, and the health insurance exchanges created by the Affordable Care Act (ACA). These therapies have the potential to offer substantial improvement over existing therapies used to treat serious or life-threatening diseases or conditions and receive priority and / or expedited review by the FDA. Breakthrough therapies represent only a small subset of the estimated 5,400 medications in the clinical development pipeline.[3]

The 10 selected medications are likely to result in medication costs to the government of $49.3 billion over a 10-year period, including: $31.3 billion in Medicare spend; $15.8 billion in state and federal Medicaid spend; and $2.1 billion as a result of subsidies provided through exchange plans. Overall, Medicare has the largest exposure to the medications analyzed, accounting for approximately 63 percent of the total costs projected in the analysis; however, the impact to individual government payers will vary by medication.

Over 10 years, total U.S. spending may exceed these estimates because the analysis does not: 1) include the impact on government programs other than those identified above; 2) evaluate the potential impact on commercial payers or patient out-of-pocket costs (OOP); or 3) consider costs potentially attributable to off-label use of medications, which can be significant.

Finally, estimates reflect the gross cost of new medication use. This analysis does not: 1) consider savings or additional costs associated with other potential medical or pharmaceutical spending as a result of new medication utilization, or 2) explicitly evaluate the impact of payer coverage policies and OOP costs on patient access. Assumptions and additional limitations are reviewed in the full text below.

INTRODUCTION

The rapid evolution of pharmaceutical innovation requires government payers—as well as the health plans and providers that serve these programs—to anticipate the launch of new products and evaluate how they may impact costs. The discussion that follows considers the potential impact of 10 breakthrough designated therapies on costs for three government programs.
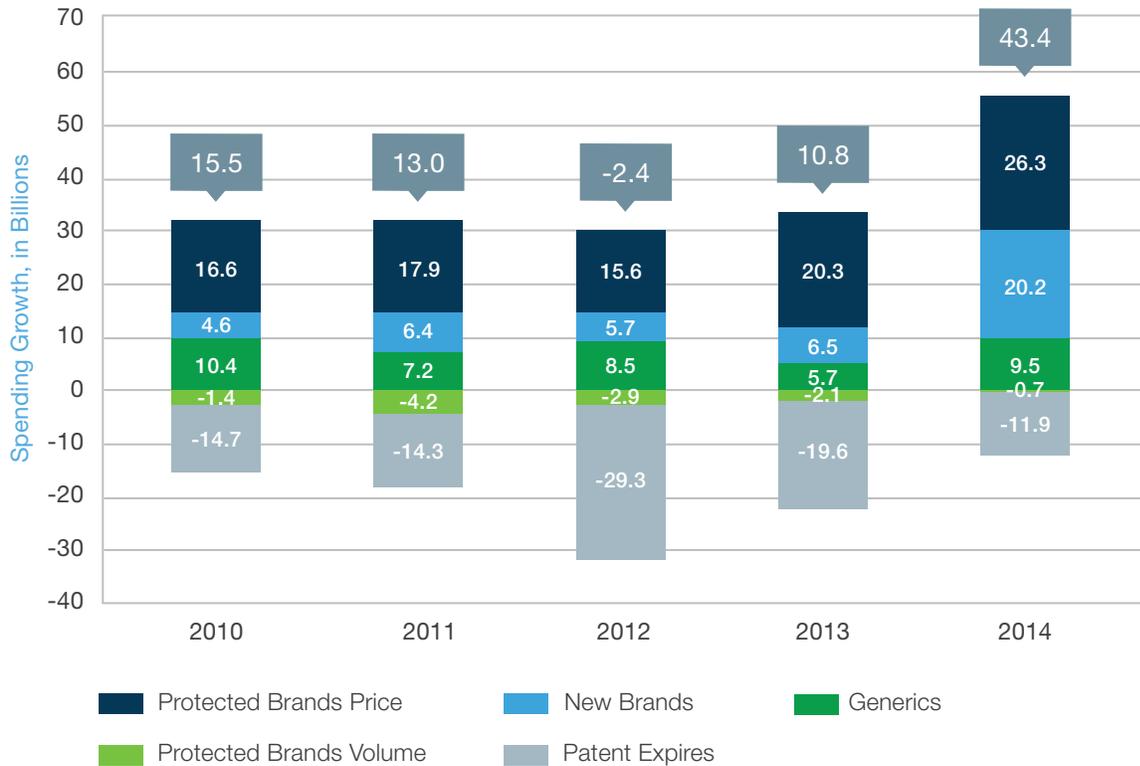
U.S. Healthcare Spending and the Role of Prescription Drugs

National health spending comprises several components, including hospital care, physician services, nursing facilities, durable medical equipment, and prescription drugs. In 2013, retail drugs represented 9.3 percent of total national health expenditures, not accounting for drugs purchased outside the retail setting, such as those used in hospitals or other facilities.[4] When accounting for nonretail spending, the Altarum Institute estimates that drug costs represented approximately 13 percent of national health expenditures in 2013 or $381 billion.[5]

Overall, the portion of national health spending attributable to prescription drugs has remained relatively constant in recent years.[6] This is because, over time, increased reliance on generics and the loss of patent exclusivity for drugs that were widely used helped keep overall drug trend low, despite new specialty products entering the market.[7] Nevertheless, drug spending grew significantly in 2014 over 2013 levels.[8] The IMS Institute for Healthcare Informatics reports a 13.1 percent overall growth rate in drug spending between 2013 and 2014, not accounting for manufacturer rebates.[9] Nearly half of this growth—6.1 percentage points—is attributable to new products entering the market over the past two years. In particular, specialty medications accounted for 78 percent of the $20.2 billion increase in new brand spending in 2014.[10]

Looking ahead, this trend is likely to continue, with specialty drug spending projected to increase, while the overall proportion of healthcare spending attributable to drugs remains relatively constant. Specifically, between 2014 and 2023, the nation is projected to spend nearly $40 trillion on healthcare, with the combination of retail and nonretail drug spending representing between 13 and 13.5 percent of costs each year during this time.[11] Meanwhile, pharmacy benefit managers generally agree that specialty drug spending is likely to increase between 15 percent and 20 percent from 2015 to 2016.[12]

Figure 1: U.S. Drug Spending Growth Drivers, 2010-2014, in Billions

Year	Patent Expires (top)	Protected Brands Price	New Brands	Generics	Protected Brands Volume	Patent Expires
2010	15.5	16.6	4.6	10.4	-1.4	-14.7
2011	13.0	17.9	6.4	7.2	-4.2	-14.3
2012	-2.4	15.6	5.7	8.5	-2.9	-29.3
2013	10.8	20.3	6.5	5.7	-2.1	-19.6
2014	43.4	26.3	20.2	9.5	-0.7	-11.9

Y-axis: Spending Growth, in Billions

Legend:
- Protected Brands Price
- Protected Brands Volume
- New Brands
- Patent Expires
- Generics

Source: IMS Health, National Sales Perspective, December 2014.
New Brands includes products launched in the last two years.

Impact of Breakthrough Therapies

To help innovative therapies reach patients sooner, Congress gave the FDA authority in the Food and Drug Administration Safety and Innovation Act (FDASIA)[13] of 2012 to establish the breakthrough therapy designation to speed development and review of certain drugs to treat serious or life-threatening conditions.[14, 15] Per FDASIA, upon request of a drug developer, FDA may designate a drug as a breakthrough therapy if it is:

> *"Intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development."*[16]

The breakthrough therapy designation brings significant advantages for drug developers, including:

- **Intensive guidance on efficient drug development,** which FDA contemplates may lead to smaller or shorter clinical trials;

- **Organizational commitment,** which includes proactive and collaborative involvement of senior FDA staff; and

- **Eligibility for rolling review,** which means FDA will review portions of the marketing application prior to submission of the complete application.

Applications for approval of designated breakthrough therapies may also be eligible for "priority review," another of FDA's expedited programs that aims to shorten the time FDA takes to review and make a decision on an application.[17] FDA's goal to decide on a "standard" application is 10 months, a "priority review" shortens that goal time to 6 months.[18] Further, for some breakthrough therapy designated products granted priority review, the FDA may grant "expedited review" in which the FDA intends to decide on the application at least one month in advance of the goal date, further shortening review times.[19] In 2014, 51 therapies were approved by the FDA, of which 9 were designated breakthrough therapies. These 9 breakthrough therapies completed review by the FDA in an average of 4 months, compared to roughly 16 months for other drugs approved in 2014.[20]

The most well-known breakthrough therapy to date is Sovaldi®, the curative therapy approved in 2013 for the treatment of hepatitis C. Via its breakthrough designation, Sovaldi received market approval in eight months.[21, 22] With approximately three million people estimated to suffer from hepatitis C in the U.S., the value of a therapy with a very high cure rate and the potential to significantly reduce side effects of treatment represented a meaningful clinical advance for affected patients.[23] For years, expensive, innovative therapies did not engender the same criticism as Sovaldi because of their relatively small patient population. Looking ahead, therapies that come with a high cost *and* serve a large patient population are most likely to have an impact on government costs and consumer premiums.

Breakthrough Therapies as Part of the Overall Pipeline

Breakthrough therapies represent only a small subset of the overall pipeline of medications that will drive prescription drug spending over the next decade. The Analysis Group reports that there are more than 5,400 medications in the clinical development pipeline, with more than half in Phase II or Phase III clinical trials.[24] While many of these therapies may never reach the U.S. market, the value of the drug development pipeline grew by nearly 46 percent between 2013 and 2014, according to EvaluatePharma.[25]

Indeed, in a recent report, EvaluatePharma documents a robust pharmaceutical pipeline that extends beyond products with breakthrough designation. Specifically, of the 20 drugs on EvaluatePharma's most valuable pipeline product list, only 9 have received a breakthrough designation from the FDA. In particular, EvaluatePharma and others point to both PD-1 cancer therapies and the cholesterol-targeting PCSK9s, which have not received breakthrough status, as new therapies likely to have a significant impact on the market in 2015 and beyond.[26] Of the most valuable pipeline products, 5 are PD-1 inhibitors, 2 are PCSK9 inhibitors, and 2 are CDK inhibitors. Overall, the report projects a sustained period of growth for the industry.[27]

PROJECT PURPOSE

As a result of the trends described above, lawmakers, industry stakeholders, and consumers have posed several important questions including: What other medications are in the pipeline? What diseases will these medications treat? What will be the costs associated with these medications? How will payers, particularly government payers, be impacted if these medications reach the market?

To begin to address these questions, Avalere analyzed breakthrough therapies to:

- **Identify and anticipate** a subset of new therapies expected to come to market that are likely to have a significant impact on government costs; and

- **Estimate the fiscal impact** of these drugs on public payers, including Medicare, Medicaid, and ACA exchanges.

Breakthrough therapies were chosen for the analysis because the designation offers a defined universe of medications for consideration; these medications also have an expedited timeline for approval. In addition, breakthrough medications are generally expected to command high prices from the market, given the value they are likely to deliver to patients.

While new therapies are likely to have a significant impact on payers other than those identified above, commercial payers, employers, and other government entities, such as the Departments of Veterans Affairs and Defense, are excluded from this analysis.

METHODOLOGY

To address these questions, Avalere engaged in a multi-step analysis, which included:

| Selecting the medications used for the analysis | Projecting the likely payer mix for each medication | Estimating a price for each medication | Projecting potential utilization for each medication |

Selecting Medications

To select the medications for use in the analysis, Avalere identified a total of 55 medications designated as breakthrough therapies and announced by the respective manufacturers as of November 2014. To reduce the list from 55 to 10, Avalere first eliminated medications that had been approved for their breakthrough indication and entered the market as of November 2014.[i] Next, each medication was assigned a projected yearly sales figure based on a combination of publicly available data, including industry reports and trade publications, as well as private interviews with financial analysts.[ii] Avalere then estimated the projected time to market for a product based on clinical development status and public announcements from manufacturers.[28] Products were selected for analysis that were likely to generate the highest revenue over the next 10 years by multiplying the yearly projected sales by the number of years the product is projected to be on the market between 2015 and 2024. The 10 medications with the highest potential revenue based on this initial assessment were chosen for inclusion in the analysis.

Projecting Payer Mix

To arrive at a payer mix for each of the medications selected for the analysis, Avalere used surveys conducted by the National Center for Health Statistics (NCHS) that provide a national sample of medical visits[29] and the National Health and Nutrition Examination Survey (NHANES) that assesses the health status of adults and children in the U.S.[30] We queried the NCHS and NHANES survey data using ICD-9-CM diagnosis codes for disease states addressed by the 10 selected products:

- Hepatitis C: 070.44, 070.54, 070.70, 070.71, V02.62;

- Cystic Fibrosis: 277.00 – 277.09;

- Breast Cancer: 174.0 – 174.9, 175.0 – 175.9;

- Lung Cancer: 162.3 – 162.9;

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i   Twenty drugs on this list have been approved for their breakthrough indications and 2 drugs have since lost breakthrough designation. These 2 drugs are included in the 10 drugs selected for analysis.

ii   Note: Sales figures were used as proxies for product selection only. Actual price and utilization assumptions for the purposes of the government payer analysis vary and are discussed elsewhere in the methodology section.

- Acute Lymphocytic Leukemia (ALL): 204.00, 204.01, or 204.02; and

- Diabetic Retinopathy: 362.01 – 362.07.

Based on these findings, Avalere utilized its proprietary enrollment model to project how each payer mix would shift over the 10-year window included in the analysis. The model takes into account a number of factors, including: the effects of an aging population;[iii,31] trends in employer-sponsored insurance; and the coverage shifts resulting from the coverage expansions included as part of the ACA. Multiple data sources inform the model, including: the Congressional Budget Office (CBO), Department of Health & Human Services (HHS), Centers for Medicare & Medicaid Services (CMS), Census Bureau, American Community Survey, Medical Expenditure Panel Survey (MEPS), Medicare Current Beneficiary Survey (MCBS), and others.

Table 1: Medications Included in Analysis

Drug	Disease	Indication	Projected Launch Date*	Current Development Status
Viekira Pak™	Hepatitis C	Hepatitis C (Genotype 1)	On market	Approved December 19, 2014
Ibrance®	Breast Cancer	Post-menopausal women with locally advanced or metastatic breast cancer ER+, HER2-	On market	Approved February 3, 2015
Eylea®	Diabetic Retinopathy	Diabetic retinopathy in patients with diabetic macular edema	On market	Approved March 25, 2015
Kalydeco™	Cystic Fibrosis	Cystic Fibrosis in patients aged 12 and older, homozygous for the F508delta mutation in CFTR	2016	NDA submitted
Keytruda®	Lung Cancer	EGFR-negative & ALK rearrangement-negative NSCLC	2017**	Phase III
MK-5172	Hepatitis C	Hepatitis C (Genotype 1)	2017***	Phase III

iii   The model projects the impact of an aging population on a disease specific payer mix, but does not adjust the projected disease specific payer mix to account for changes in the demographic characteristics of the specific patient population. Modifications were made to the model to reflect the impact of the age cohort demographics of the hepatitis C population on the payer mix over the next 10 years. Three-fourths of the hepatitis C population was born between 1945 and 1965; thus, a majority will age into Medicare from 2015 to 2024.

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Drug	Disease	Indication	Projected Launch Date*	Current Development Status
Entinostat	Breast Cancer	Locally recurrent or metastatic ER+ breast cancer when added to exemestane in postmenopausal women whose disease has progressed following non-steroidal aromatase inhibitor therapy	2018	Phase III
Rociletinib	Lung Cancer	Second-line treatment of EGFR mutant NSCLC with T790M mutation	2018	Phase III
Daclatasvir	Hepatitis C	Hepatitis C (Genotype 1b)	2018	Phase III
CTL019	Acute Lymphoblastic Leukemia (ALL)	Pediatric and adult patients with elapsed/refractory ALL	2020	Phase II

ALK: Anaplastic Lymphoma Kinase   CFTR: Cystic Fibrosis Transmembrane Conductance Regulator   EGFR: Epidermal Growth Factor Receptor   ER+: Estrogen Receptor Positive   HER2: Human Epidermal Growth Factor Receptor 2   NSCLC: Non–Small Cell Lung Cancer

* Based on FDA time for acceptance and priority review once the application is submitted as well as general R&D timelines available here: "Drug Discovery and Development: Understanding the R&D Process." Washington, DC: PhRMA, 2014.

**Keytruda was initially assumed to have a 2018 launch given Phase III clinical trial status, but the manufacturer has said it intends to file for approval in 2015. Given a competitor, Opdivo®, has recently been approved for this indication, it is assumed that the approval timeline will be 12+ months from the file date without priority status.

*** MK-5172 was initially assumed to have a 2018 launch given Phase III clinical trial status, but the manufacturer has said it intends to file for approval in 2015. Given other competitors in the market, it is assumed that the approval timeline will be 12+ months from the file date without priority status.

Assessing Costs: Price And Utilization

After establishing a payer mix for each medication, Avalere identified current and future prices for each drug as well as the likely utilization of each product.

Estimating Price

To determine the price used in the analysis, Avalere relied upon financial analyst reports and interviews; the pricing of close competitors or existing therapies on the market; and the existing market prices for other indications already approved, adjusted for specific dosing, where available and applicable. In all cases where prices were benchmarked to existing on-market products, including those drugs that were approved following the November

2014 cutoff for drug selection, Avalere utilized the current Wholesale Acquisition Cost (WAC) pricing for a base patient using the anticipated dosing regimen.[32] To project future price variation, Avalere used the Consumer Price Index (CPI) for prescription drugs prepared by the Bureau of Labor Statistics (BLS), specifically applying the most recent 5-year historical average growth rate over the 10-year analysis window.[33] Avalere assumed no specific pricing impacts from market competition in the future, with the exception of rebates described below.

Both regulation and market practice often require manufacturers to provide rebates to payers. Avalere assumed a standard Medicaid rebate for brand products (23.1 percent) as well as supplemental rebates for hepatitis C products where publicly available information exists.[34] For Medicare Part D, Avalere assumed the average 15 percent rebate reported by the CBO.[35] This level of commercial rebate is in line with reports of average rebates obtained by plan sponsors for brand drugs under a pharmacy benefit (16-18 percent).[36] The same 15 percent rebate was applied to the exchange market for drugs accessed through the pharmacy benefit. Finally, Avalere assumed no rebate for medical benefit drugs reimbursed through Medicare Part B or accessed through exchange plans.

In order to appropriately calculate rebates, Avalere cross-walked each product's WAC to Average Wholesale Price (AWP), Average Manufacturer Price (AMP), and Average Sales Price (ASP) based on the interactions between those different price types.[37]

Projecting Utilization

Utilization assumptions are specific to each medication's clinical indication and adjusted based on a variety of factors, including: potential competition in the marketplace;[38, 39] projected take-up rate using available literature;[40-43] population growth based on the demographics associated with the condition;[44] new cases year-over-year (incidence) and patient mortality;[45-53] and treatment length.[54-58]

PROJECTED PAYER MIX

Growing Role of Government Payers

The ACA and changing demographics create an increasing role for government payers in the coming years (see **Figure 2**). Specifically, the implementation of health insurance exchanges and the Medicaid expansion under the ACA will lead to significant shifts into government-sponsored markets as well as a reduction in uninsured Americans. Meanwhile, the "baby boom" generation is expected to age into the Medicare program, accelerating enrollment. Despite these trends, employer coverage will remain the largest single source of health insurance coverage for Americans.

Figure 2: Projected Enrollment By Payer Type, 2013 & 2017, in Millions
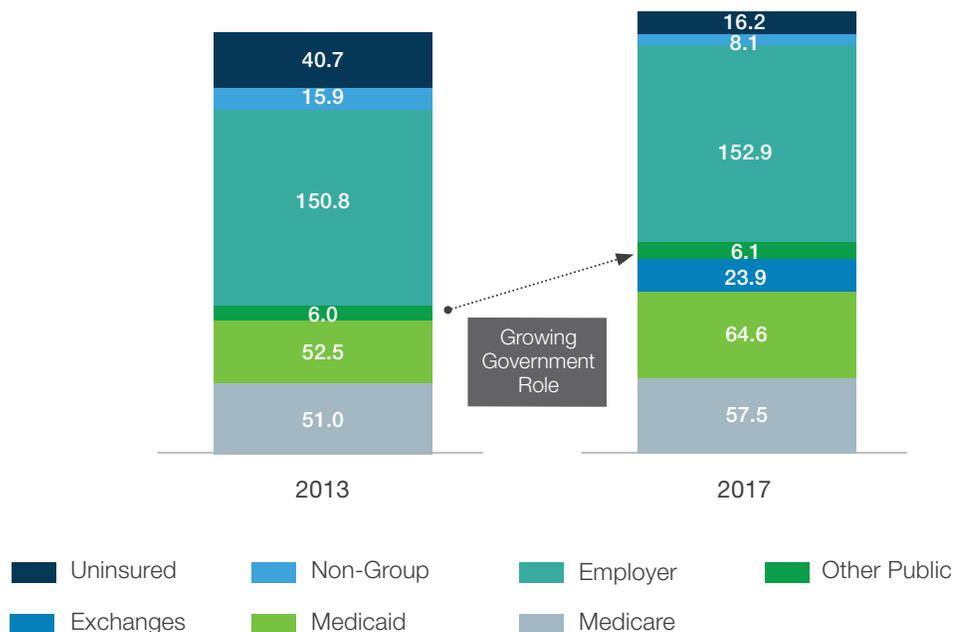
Source: Avalere All-Payer Enrollment Model. Medicaid expansion scenarios based on latest state decisions. October 1, 2014.

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Role of Medicare, Medicaid, and Exchanges

The discussion below focuses on the exposure of Medicare, Medicaid, and ACA exchanges to the 10 breakthrough therapies chosen for the analysis. The combination of these three major government payers will be responsible for a significant portion of people projected to utilize the selected therapies, with specific percentages ranging from nearly 47 percent for Kalydeco up to 77 percent for Keytruda (see **Table 2**).

Table 2: Projected Payer Mix of Selected Therapies, 2024

	Major Government Payers				
Drug	**Medicare**	**Medicaid**	**Exchanges***	**Total**	**Other**
Viekira Pak	55.8%	7.7%	2.0%	65.5%	34.5%
Ibrance	38.5%	8.0%	1.8%	48.2%	51.8%
Eylea	59.5%	7.8%	1.4%	68.7%	31.3%
Kalydeco	4.0%	40.0%	2.8%	46.8%	53.2%
Keytruda	69.6%	6.9%	0.5%	77.0%	23.0%
MK5172	55.8%	7.7%	2.0%	65.5%	34.5%
Entinostat	38.5%	8.0%	1.8%	48.2%	51.8%
Rociletinib	55.9%	6.9%	0.5%	63.3%	36.7%
Daclatasvir	55.8%	7.7%	2.0%	65.5%	34.5%
CTL019	8.9%	42.9%	2.8%	54.5%	45.5%

*Government costs incurred through tax credit subsidies and cost-sharing reductions. Source: Avalere analysis, 2015.

Payer mix is driven by a number of factors, including, but not limited to the:

- Prevalence, incidence, and mortality of the disease a medication is used to treat;

- Age and income of people with the condition;

- Impact of policy changes, such as the ACA, on source of coverage;

- Rates at which a disease is diagnosed and treated; and

- Rate at which individuals take advantage of, or "take up," available treatment options as influenced by benefit design and price elasticity.

Table 2 above demonstrates that the relative exposure of government payers to different therapies can vary significantly. For example, Kalydeco is indicated for cystic fibrosis patients over the age of 12. More than 75 percent of cystic fibrosis patients are diagnosed by the age of two, yet patient life expectancy is shorter than the average population.[59] Not surprisingly, therefore, potential Medicare exposure to Kalydeco is low compared to other therapies; however, exposure to Medicaid is high, given the robust coverage of children through Medicaid and the Children's Health Insurance Program (CHIP). Conversely, Keytruda is indicated for late-stage lung cancer, which is typically diagnosed later in life. Indeed, 82 percent of people living with lung cancer are over the age of 60.[60] As a result, Keytruda's projected Medicare exposure is high at nearly 70 percent.

PROJECTED COST TO GOVERNMENT

Based on the payer mix described above, Avalere assessed the potential impact of the 10 breakthrough therapies included in this analysis on three government payers—Medicaid, Medicare, and exchanges—over a 10-year period between 2015 and 2024. The cost impact to government payers excludes the amounts paid by consumers as described below. Note that the analysis for each program includes only the projected aggregate pharmaceutical cost for these 10 products. Avalere did not attempt to estimate the decrease or increase in medical or other pharmaceutical spending that might be associated with the use of the product, the effect on government costs as result of increased longevity, effects on labor markets, consumer surplus, or any other secondary effects.

Medicare

Future Medicare Program Growth

Despite a recent slowdown in Medicare cost growth, 76 million[61] aging baby boomers are projected to increase Medicare enrollment and costs to government over the coming years. Avalere projects total Medicare enrollment will grow from 51 million in 2013 to 57.5 million in 2017.

Medicare Parts B and D

In general, the federal government incurs Medicare costs by providing both medical and pharmacy benefits implemented through a combination of fee-for-service reimbursement and managed care programs, including Medicare Advantage (MA) and Part D. Specifically, to provide necessary medications to Medicare beneficiaries, Medicare pays for:

- **Medical benefit drugs that are administered in a physician office or hospital outpatient setting**—these drugs are typically injected or infused and covered under Medicare Part B; and

- **Pharmacy benefit drugs that are self-administered**—these drugs are usually oral, topical, or self-injectable and are covered under Medicare Part D.

Roughly 30 percent of Medicare beneficiaries enrolled in Part B receive their benefits from MA plans and roughly 38 percent of all Part D enrollees are enrolled in MA plans that provide medical and prescription drug coverage (MA-PD plans).[62]

Medicare Part B: Reimbursement and Patient Cost Sharing

Medicare reimbursement and patient cost-sharing structures differ for medications covered under Parts B and D. Specifically, Medicare reimburses providers at 106 percent of the ASP

of the drug for Part B covered drugs. Of this amount, in general, the federal government pays 80 percent, while beneficiaries are responsible for 20 percent. Nevertheless, under the sequester, effective March 2013 through 2021, the Medicare portion is reduced by 2 percent.[63] Thus, the resulting federal government share is about 78.4 percent of the posted ASP plus 6 percent rate. The federal government amount was further adjusted to account for beneficiary-paid premiums and state government contributions for dual eligibles for Part B premiums and cost sharing. Medicare imposes no mandatory rebates for Part B drugs, and current industry practice generally does not include voluntary rebates. Three drugs (Keytruda, Eylea, and CTL019) included in this analysis are expected to be covered under Medicare Part B and reimbursed under payers' medical benefit.

Medicare Part D: Reimbursement and Patient Cost Sharing

The federal government finances approximately 75 percent of Medicare Part D costs through a combination of direct risk-adjusted subsidies, reinsurance for beneficiary spending beyond the OOP maximum, and payments to plans to cover nearly all of premiums and cost sharing for low-income subsidy recipients (LIS).[64] However, under the Part D program, plans negotiate reimbursement amounts directly with manufacturers, unlike under Part B.

In general, patient cost sharing under Part D varies by plan. However, every year the Part D program defines a standard benefit. Plans must offer benefit designs actuarially equivalent to the standard benefit; plans can also offer enhanced benefits.

The Part D 2015 standard benefit includes a $320 deductible followed by 25 percent coinsurance, on average, until an enrollee reaches an initial coverage limit of $2,960. Actual cost sharing varies by plan selection and drug tier placement, among other factors. Above the initial limit but below the OOP threshold of $4,700 is a coverage gap, known as the "donut hole," where Part D enrollees had historically been responsible for 100 percent of drug costs. The ACA, however, gradually closes the donut hole, in part, by requiring manufacturers of brand-name drugs to provide a 50 percent rebate on sales in the gap.[65] Above the OOP threshold, Part D enrollees are generally responsible for 5 percent coinsurance. Avalere used its proprietary Part D OOP calculator to determine consumer cost sharing for the purposes of this analysis, assuming all included Part D drugs were placed on the specialty formulary tier.[iv]

Unlike Part B, manufacturers do generally provide voluntary rebates to Medicare Part D plans as part of the normal negotiation process with health insurers. For the purposes of this analysis, Avalere assumed Part D plans receive an average manufacturer rebate of 15 percent, as per CBO estimates.[66] Seven drugs included in the analysis (Viekira Pak, Ibrance, Kalydeco, MK5172, entinostat, rociletinib, and daclatasvir) are expected to be covered under Medicare Part D and plans' pharmacy benefit.

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iv Under Part D, Avalere also assumed the federal government pays the full estimated drug cost for LIS beneficiaries due to minimal contributions to premiums and copays from that population. For non-LIS beneficiaries, Avalere calculated annual drug costs using Avalere's proprietary Part D calculator and then applied 74.5 percent which is an estimated, average federal government's share of Medicare Part D costs.

v The State portion of Medicaid costs for Part B premiums and cost sharing for dual eligibles are included under the State portion of Medicaid spending.

## Figure 3: Medicare Costs, 2015-2024, in Billions
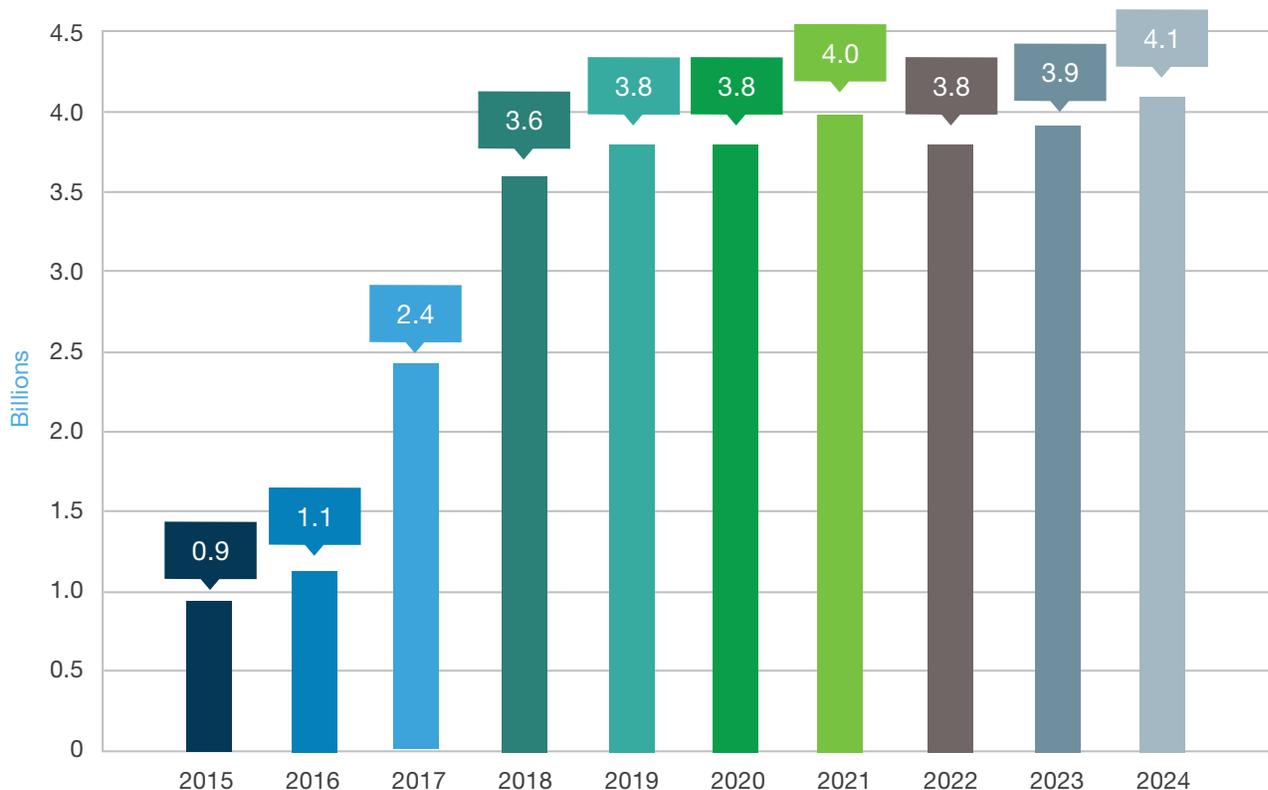
Note: Figures may not add due to rounding.
Source: Avalere analysis, June 2015.

Projected Costs to Medicare

Figure 3 shows that the 10 breakthrough therapies selected for this analysis are projected to cost the Medicare program $31.3 billion over the 10-year period spanning from 2015 to 2024. Specifically, annual costs range from $900 million in 2015 to $4.1 billion in 2024. These figures include applicable costs incurred through Medicare Part B, MA, and Part D, including the spending associated with providing prescription drug coverage to dual eligibles covered by both Medicare and Medicaid.[v]

Figure 4: Projected Medicaid Enrollment, 2013-2017, in Millions
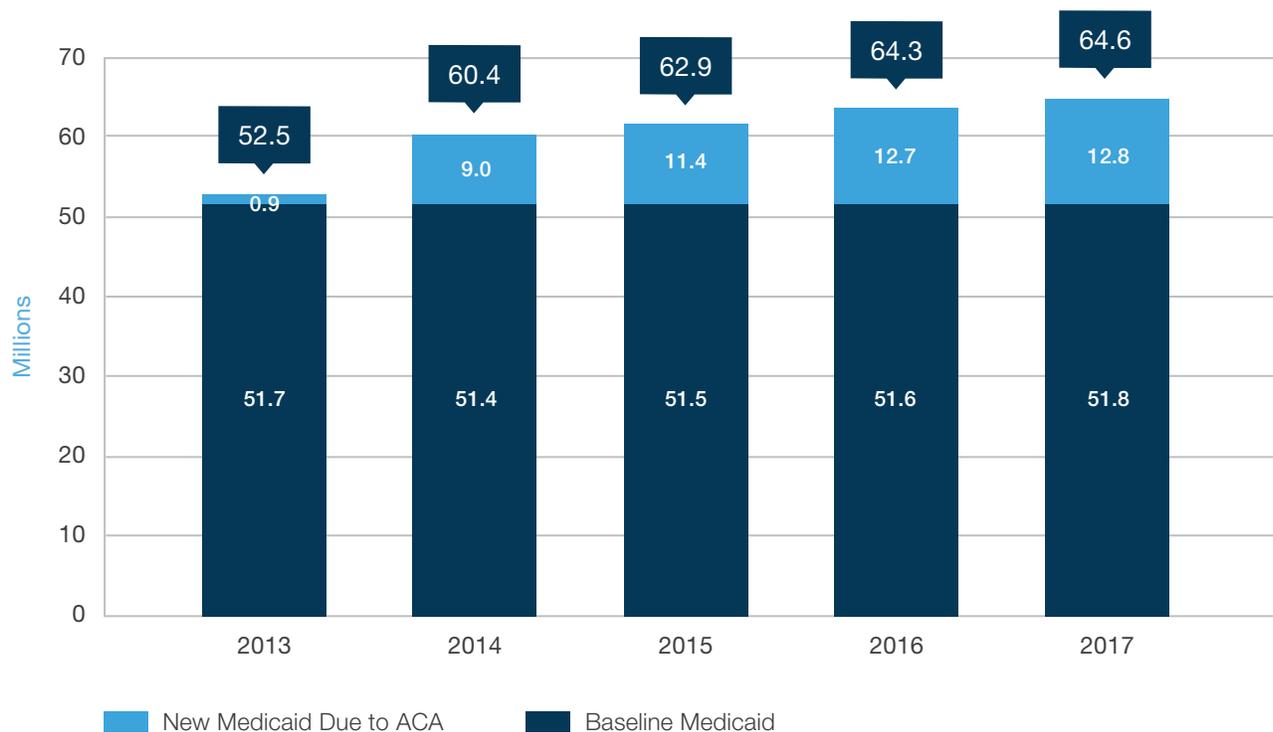
Source: Avalere All-Payer Enrollment Model. Medicaid expansion scenarios based on latest state decisions. October 1, 2014.

Medicaid

Program Growth Under the Affordable Care Act

The ACA included a significant Medicaid expansion for individuals categorically eligible up to 138 percent of the federal poverty level (FPL). While the Supreme Court made the expansion optional, 28 states and the District of Columbia have committed to expanding the program under the ACA.[67] As a result of states' expansion decisions and the so-called "woodwork effect," the Medicaid program is expected to grow significantly over the coming years. As shown in **Figure 4**, between 2013 and 2017 Medicaid enrollment is projected to increase by 23 percent because of the ACA.

Reimbursement and Patient Cost Sharing

Medicaid program costs accrue to both state and federal governments. Specifically, each state has an established Federal Medical Assistance Percentage (FMAP). A state's FMAP determines its federal "match"—the number of federal dollars provided to a state for each

dollar in state Medicaid spending.[68] For 2015, state FMAPs range from 50 percent in 13 states, including California and New York, to 73.6 percent in Mississippi.[69] However, the ACA included an enhanced FMAP to help finance costs associated with the Medicaid expansion population. Specifically, the ACA includes a 100 percent FMAP for the expansion population in 2014, 2015, and 2016 that gradually declines to 90 percent in 2020.[70] To calculate Medicaid program costs that would accrue to both state and federal governments, Avalere used the average FMAP rate of 57 percent across states for Medicaid beneficiaries eligible prior to the ACA, and the enhanced FMAP described above for the expansion population.[71-74]

All states offer prescription drug coverage to their Medicaid beneficiaries, though it is technically optional under federal law. In contrast to Medicare, the Medicaid program includes a mandatory rebate program. Specifically, in order for Medicaid to cover a brand drug, manufacturers must pay a statutory minimum rebate on sales to Medicaid beneficiaries, which equals:

- The higher of 23.1 percent of AMP, the average price manufacturers receive on sales to retail pharmacies; or

- AMP minus Best Price (BP), the lowest single price paid by almost any purchaser in the U.S.[75]

Manufacturers are required to pay an additional rebate when increases in the AMP of a product exceed the rate of inflation. This is also known as the "inflation penalty" or CPI rebate.[76] In addition, states and Medicaid managed care plans may negotiate supplemental rebates with manufacturers.

For the purposes of this analysis, Avalere assumed the standard 23.1 percent Medicaid rebate. In general, the analysis does not account for supplemental rebates, with the exception of drugs used to treat hepatitis C, where strong market competition has driven deeper price concessions and publicly available rebate data is available.[vi] In general, 8 percent of the rebate amount accrues to the federal government, with 15.1 percent split between the federal and state governments according to a state's FMAP. Therefore, Medicaid rebates for the expansion population will accrue 100 percent to the federal government through 2016.

In general, Medicaid requires minimal financial contribution from beneficiaries. While states may impose premiums along with copayments, coinsurance, and deductibles, cost sharing for most services is restricted to nominal amounts. To date, many states impose no cost sharing in the Medicaid program.[77] As a result, Avalere assumed consumers enrolled in Medicaid will incur no cost sharing when accessing medications.

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vi   As a result, findings may over estimate Medicaid costs associated with the selected therapies.

vii   The State portion of Medicaid costs for Part B premiums and cost sharing for dual eligibles are included under the State portion of Medicaid spending.

Figure 5: Medicaid Costs, 2015-2024, in Billions
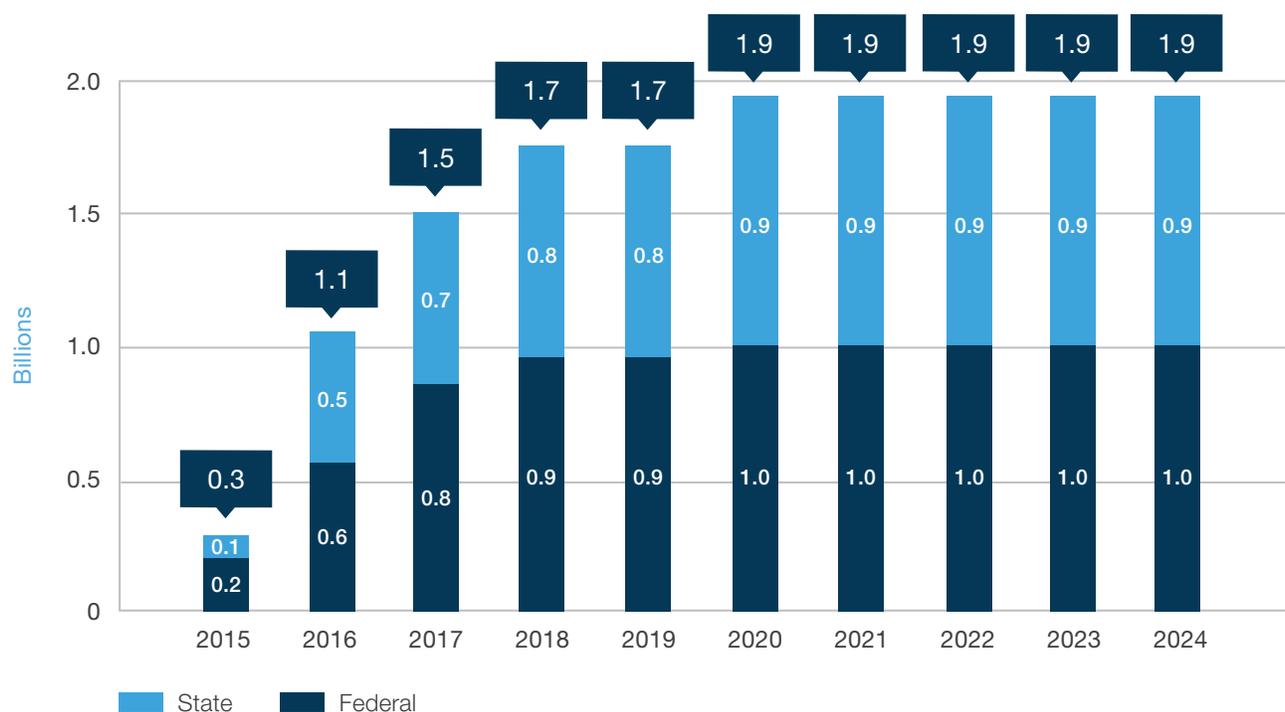
Source: Avalere analysis, June 2015.

Projected Costs to Medicaid

As shown in **Figure 5**, Avalere projects the 10 therapies selected for this analysis will cost the Medicaid program $15.8 billion—$8.4 billion in federal and $7.4 billion in state costs respectively—over the next 10 years. For the 10 drugs analyzed, projected annual Medicaid costs to state and federal governments range from $300 million in 2015 to $1.9 billion between 2020 and 2024.[vii]

Table 3: Actuarial Value Organized by Metal Level

Metal Level	Actuarial Value (AV)
Bronze	60% AV
Silver	70% AV
Gold	80% AV
Platinum	90% AV

Source: Section 1302 of the ACA.

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Public Exchanges

The Emerging Public Exchange Market

In addition to expanding Medicaid, the ACA established health insurance exchanges to facilitate access to affordable insurance for individuals and small businesses. Exchanges offer consumers the opportunity to choose among a variety of private health plans that are required to adhere to established actuarial value standards and Essential Health Benefits (EHB). Specifically, health plans offered on the exchange are organized by metal level as shown in **Table 3**.

In addition, EHB requires plans to cover 10 categories of coverage, including prescription drugs. As of the end of the 2015 open enrollment period, 11.7 million people are enrolled in exchanges throughout the country, with 67 percent enrolling in Silver plans.[78] Avalere projects that total exchange enrollment will reach 24 million by 2017.

Patient Cost Sharing in Exchanges

In addition to implementing insurance market reforms to make coverage accessible for consumers, the ACA provides premium tax credits and cost-sharing reductions (CSRs) to increase the affordability of insurance through the newly established exchanges. As a result, premium tax credits and CSRs created by the ACA drive federal government costs related to exchanges.

Table 4: Premium Subsidies to Limit Premium Spending as a Percent of Income for Individuals Under 400% FPL [ix]

Income	Premiums Limited to % of Income
100–133% FPL	2.0%
133–150% FPL	3.0–4.0%
150–200% FPL	4.0–6.3%
200–250% FPL	6.3–8.05%
250–300% FPL	8.05–9.5%
300–400% FPL	9.5%

Source: Section 1401 of the ACA.

viii   Defined as 60 percent AV.

ix   Applies to the second lowest cost Silver plan available in the exchange.

Tax Credits in Exchanges

Specifically, the ACA provides tax credits to individuals between 100 and 400 percent of the FPL who do not have access to affordable, minimum value[viii] coverage through their employer or other government program, such as Medicaid. Specifically, the tax credits cap monthly premium contributions at a percentage of income (see **Table 4**), limiting consumer liability and requiring the federal government to finance any excess costs.

The vast majority of exchange consumers are subsidized at a very high rate. Roughly 87 percent of exchange enrollees receive a tax credit subsidy, with the average subsidy paying for 72 percent of premium costs.[79] Avalere projects 19 million individuals will receive subsidies through exchanges by 2017.

Table 5: Cost-Sharing Subsidies for Individuals with Incomes Below 250% FPL

| Household Income	Individual OOP Cap for 2015	Individual OOP Cap for 2016	Family OOP Cap for 2015	Family OOP Cap for 2016	Actuarial Value
100–150% FPL	$2,250	$2,250	$4,500	$4,500	94%
150–200% FPL	$2,250	$2,250	$4,500	$4,500	87%
200–250% FPL	$5,200	$5,450	$10,400	$10,900	73%
250–400% FPL	$6,600	$6,850	$13,200	$13,700	70%

Source: HHS Notice of Benefit and Payment Parameters for 2015 and 2016.

Cost-Sharing Reductions

In addition, the ACA provides CSRs to individuals between 100 and 250 percent of the FPL to reduce OOP costs. While health plans have latitude in implementing CSRs, specific reductions in OOP maximums are required, as described below (see **Table 5**). Exchange consumers must enroll in a Silver plan to gain access to CSRs.

For the purposes of this analysis, Avalere assumed all consumers enroll in Silver plans and calculated average OOP costs for pharmacy and medical benefit drugs based on a weighted average of enrollment and cost sharing by income distribution, including premium and cost-sharing subsidies.[80] Avalere used 2015 benefit designs as the basis for assumptions.

Figure 6: Federal Exchange Costs, 2015-2024, in Millions
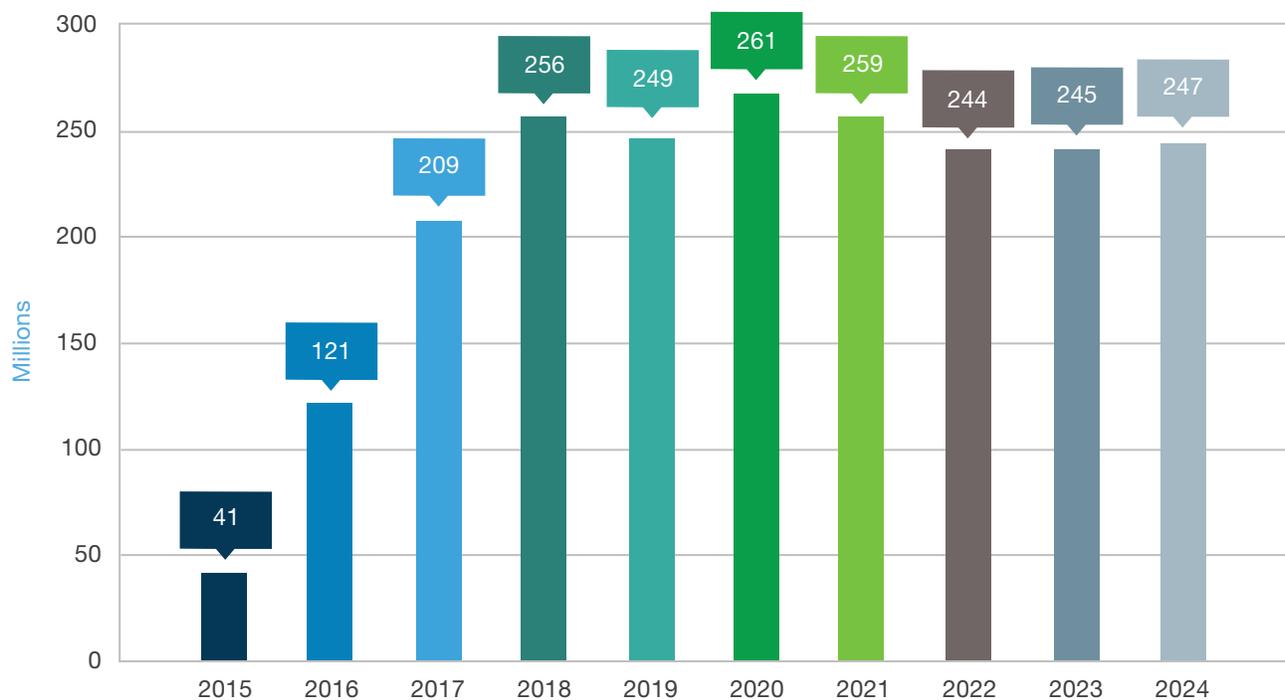
Source: Avalere analysis, June 2015.

Projected Costs to Exchanges

Over the next 10 years, the medications included in this analysis are projected to cost the federal government $2.1 billion as a result of increased exchange spending. Total yearly costs range from $41 million in 2015 to $261 million in 2020 (see **Figure 6**).

Total Costs for Medicare, Medicaid, and Exchanges

As shown in **Table 6**, Avalere finds the 10 selected medications will cost Medicare, Medicaid, and public exchanges $49.3 billion over a 10-year period, including: $31.3 billion in Medicare costs; $15.8 billion in state and federal Medicaid costs; and $2.1 billion as a result of subsidies provided through exchange plans.[x] Yearly costs are generally expected to increase over this time period, growing from $1.2 billion in 2015 to $6.3 billion in 2024. The selected therapies' exposure to Medicare remains the largest driver of government liability, accounting for approximately 63 percent of total government costs included in the estimate.

x   Figures may not add due to rounding.

Other government entities, including the Veterans Administration, Department of Defense, correctional facilities, and government employee health benefit programs, would also incur costs as a result of these treatments; however, those costs are not included in this analysis nor are projected patient OOP costs. In addition, the employer tax exclusion for healthcare remains the nation's largest federal tax expenditure.[81, 82] The cost of the tax exclusion to the federal government increases as premiums rise. Neither the direct impact of these therapies on commercial premiums nor the indirect effect on government tax expenditures is included in this analysis.

In addition, the cost estimate above assumes utilization by patients for products' indication approved through the breakthrough process. Projections do not include other FDA-approved indications or off-label prescriptions, which can be significant.[83] In particular, one study quantifies off-label prescriptions to be greater than 20 percent of total prescriptions for commonly used medications.[84] Another study looking at infused chemotherapy treatment found that 30 percent of total utilization was off-label.[85] Indeed, costs associated with off-label medication use for newly approved therapies could be significant, but are not considered here.

As noted above, this analysis does not account for secondary cost effects—positive or negative—associated with medication use.

Table 6: Projected Government Costs for Select Breakthrough Therapies, 2015-2024, in Billions

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2015-2019	2020-2024	2015-2024
Federal Government Costs													
Medicare	0.9	1.1	2.4	3.6	3.8	3.8	4.0	3.8	3.9	4.1	11.8	19.6	31.3
Medicaid	0.2	0.6	0.8	0.9	0.9	1.0	1.0	1.0	1.0	1.0	3.3	5.1	8.4
Exchanges	0.0	0.1	0.2	0.3	0.2	0.3	0.3	0.2	0.2	0.2	0.9	1.3	2.1
Total Federal Government Costs	1.1	1.9	3.4	4.7	4.9	5.1	5.3	5.0	5.2	5.4	16.0	26.0	41.9
State Government Costs													
Medicaid	0.1	0.5	0.7	0.8	0.8	0.9	0.9	0.9	0.9	0.9	2.9	4.5	7.4
Total State Government Costs	0.1	0.5	0.7	0.8	0.8	0.9	0.9	0.9	0.9	0.9	2.9	4.5	7.4
Total Costs													
Total (Federal and State)	1.2	2.4	4.0	5.5	5.7	6.0	6.2	5.9	6.1	6.3	18.9	30.5	49.3

Note: Figures may not add due to rounding.
Source: Avalere analysis, June 2015.

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CONCLUSION

Avalere finds the direct product-related spending on these 10 breakthrough therapies will cost three government payers $49.3 billion over a 10-year period, including: $31.3 billion in Medicare costs; $15.8 billion in state and federal Medicaid costs; and $2.1 billion as a result of subsidies provided through exchange plans.[xi] Overall, Medicare has the largest direct product-related cost exposure to the medications analyzed, accounting for approximately 63 percent of the total costs projected in the analysis; however, the impact to individual government payers will vary by medication.

The 10 breakthrough therapies included in this analysis represent a small subset of the overall pipeline of medications that will drive prescription drug spending over the next decade. Indeed, healthcare industry stakeholders in the U.S. continue to innovate. Understanding the cost implications of emerging therapies is critical for governments, patients, and industry alike. Over time, the debate over how best to finance the cost of innovation, while preserving the incentive to bring new therapies to market, will continue to demand thoughtful leadership from both public and private stakeholders.

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xi   Figures may not add due to rounding.

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LIMITATIONS

The preceding analysis is based on a subset of breakthrough therapy medications and a specific set of assumptions.Therefore, findings have a series of limitations, which include but are not limited to the provisions listed below. Specifically, the analysis:

- Reflects spending on select breakthrough therapies and does not take into account changes in spending (positive or negative) as a result of treatment outcomes.

- Assumes all drugs reach the market. Time to market reflects historical timelines for clinical trials and speed of FDA approval under breakthrough designation.

- Utilizes available data on potential pricing; actual prices may vary.

- Assumes some rebates; actual rebates may be higher or lower than assumptions.

- Excludes the effects of the 340B Drug Pricing Program.

- Assumes all Part D government costs occur to the federal vs. state governments; assumptions for Part D clawback payments from states are not included in the analysis.

- Assumes an impact from known competitors coming to market; actual competitors in the future may vary.

- Projects exchange costs assuming all consumers enroll in Silver plans (including cost-sharing reductions).

- Assumes take-up rates based on publicly available data and literature; actual take-up rates may vary.

- Reflects costs to Medicare, Medicaid, and exchanges. The impact on the commercial market and / or other government payers is excluded from the analysis.

- Considers selected breakthrough therapies only; the analysis does not consider the potential impact of other pipeline products.

- Reflects utilization for indications approved through breakthrough designation; the analysis does not account for other FDA-approved indications.

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