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USA

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Abstract

The United States ("U.S.") accounts for the largest share of drug spending and innovation in the world, and its drug pricing regime is the most complex given its multi-payer model and unique overlay of market access requirements that collectively impact drug pricing and reimbursement decisions in the U.S.

The U.S. health care system includes both private and public health insurance coverage. Whether a drug product is covered, and at what price, is determined by each payer's coverage, coding, and payment criteria for health insurance plans. The largest government-funded programs are Medicare and Medicaid, under which plans are subject to detailed requirements set forth by statute or regulation. Private plans, which cover far more Americans than public plans, have more flexibility to make coverage and reimbursement determinations. All plans implement various cost containment measures which may impact plan beneficiaries' access to certain drug products. For Americans that either do not have insurance or have inadequate coverage to support their drug purchasing needs, a number of public safety net programs or private assistance programs (including manufacturer assistance) may be available to ensure access to needed medications.

Drug prices are highly dependent on the complexities of the U.S. drug supply chain. Between the initial manufacturing and ultimate dispensing of a given drug product, numerous transactions must take place among manufacturers, wholesalers, pharmacies, pharmacy benefit managers ("PBMs"), providers, and payers. These transactions typically involve price concessions in the form of discounts or rebates, as well as other fees. As a result, there is a significant gap between the list price a manufacturer initially sets for a drug product, and what is sometimes referred to as the "net price" – the actual amount of money received by the manufacturer.

Successful market access requires navigating this complex pricing and reimbursement system in a way that ensures drug products are available to patients, reimbursable by patients' private or public plans, and appropriately valued to ensure favorable coverage. These efforts also must comply with overlapping regulatory requirements and minimize risk related to enforcement action for violating regulatory or compliance obligations. Manufacturers should be aware of policy proposals and emerging trends that may significantly affect drug pricing and reimbursement in the U.S.

Market introduction/overview

The U.S. health care market

Health insurance

The U.S. health care system consists of a complex mix of payers and institutions.

Government-funded programs include Medicare (a federal program that primarily covers individuals 65 years of age and over) and Medicaid (a joint federal-state program that provides coverage for individuals with limited income and resources), as well as programs for military personnel, veterans, uninsured children, and others. Private health insurance, which covers 66.5% of the population, is more prevalent than public health insurance.[1] Most private insurance is offered through employer-sponsored plans; however, Americans can also purchase coverage directly. Coverage for prescription drugs is an important component of both private and government health insurance programs.

Over 90% of Americans have health insurance through such private or public plans; however, a significant number of Americans do not have any form of health insurance coverage. In 2020, the latest year for which coverage data is available, the U.S. population of 325.6 million had coverage as follows:

- 216.5 million received coverage under private plans, including 177.2 million through employment-based plans;
- 59.8 million received coverage under Medicare;
- 57.9 million received coverage under Medicaid;
- 2.92 million received coverage through the Veterans Health Administration and the Civilian Health and Medical Program within the Department of Veterans Affairs; and
- 28.0 million were uninsured.[2]

Underinsurance remains a significant challenge. Many Americans face relatively high out-of-pocket health care costs in the form of premiums, deductibles, coinsurance, and copayments required by private and government payers for covered services, as well as costs for services not covered by insurance. In 2019, people in the top 1% of out-of-pocket spending had out-of-pocket costs of $19,500 per year on average, and people in the top 10% of out-of-pocket spending had out-of-pocket costs of $5,390 per year on average.[3]

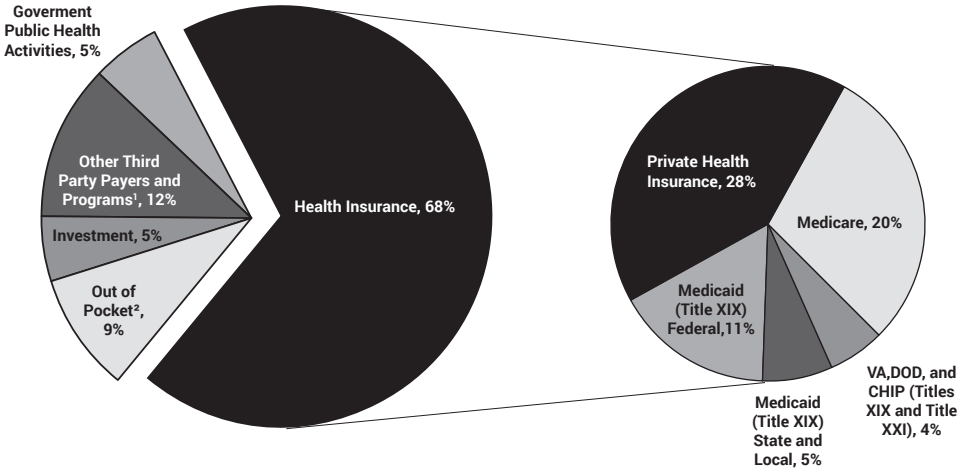
Although many developed nations choose to provide health care under a universal or single payer system, the U.S. uses a multiple payer model combined with government- and privately-run safety net programs and mandatory access to emergency care for all residents.[4] In addition to funding Medicaid and other programs aimed at vulnerable populations, the federal government requires drug manufacturers to provide outpatient drugs to health care providers that primarily serve low-income and uninsured individuals under a program known as the 340B Drug Pricing Program. Private charitable foundations also provide financial assistance or free products to eligible patients who struggle to afford expensive prescription drugs.

Health care spending

The U.S. has the highest health care spending *per capita* in the world.[5] *Per capita* spending has increased dramatically in recent decades, rising by 290% between 1980 and 2018.[6] In 2020, health care spending grew 9.7% and accounted for 19.7% of the Gross Domestic Product ("GDP").[7]

In 2020 alone, the U.S. spent approximately $4.1 trillion on health care.[8] Figures 1 and 2 show how health care spending breaks down across payers and services, as estimated by the Centers for Medicare & Medicaid Services ("CMS").

Figure 1: The nation's health dollar – where it came from[9]



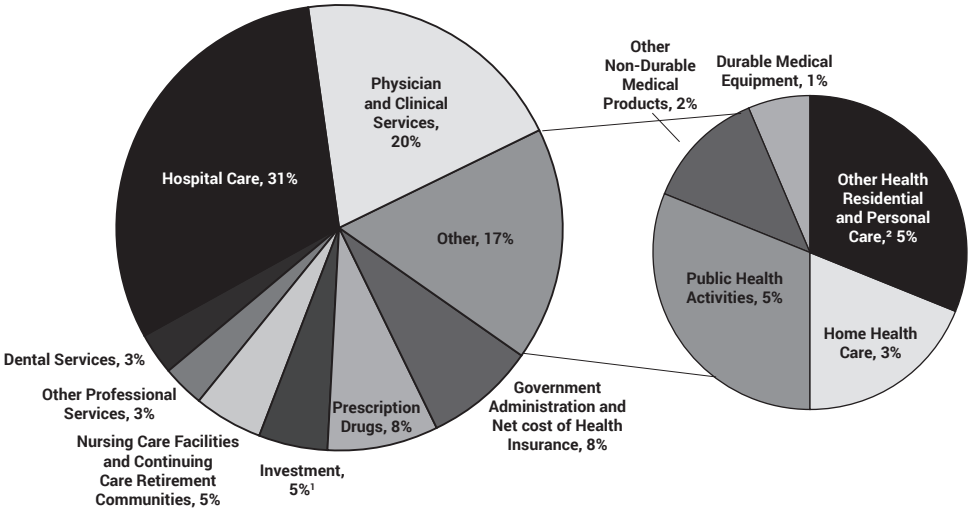
[1] Includes worksite health care, other private revenues, Indian Health Service, worker's compensation, general assistance, maternal and child health, vocational rehabilitation, Substance Abuse and Mental Health Services Administration, school health, and other federal and state local programs.

[2] Includes co-payments, deductibles, and any amounts not covered by health insurance.

Note: Sum of pieces may not equal 100% due to rounding.

SOURCE: Centers for Medicare & Medicaid Services, Office of the Actuary, National Health Statistics Group.

Figure 2: The nation's health dollar – where it went[10]



[1] Includes Noncommercial Research and Structures and Equipment.

[2] Includes expenditures for residential care facilities, ambulance providers, medical care delivered in non-traditional settings (such as community centers, senior citizens centers, schools and military field stations), and expenditures for Home and Community Waiver programs under Medicaid.

Note: Sum of pieces may not equal 100% due to rounding.

SOURCE: Centers for Medicare & Medicaid Services, Office of the Actuary, National Health Statistics Group.

As shown in Figure 2, CMS estimates that prescription drugs account for approximately 8% of health care spending. CMS estimates that, in 2020, prescription drug spending increased 3% to $348.4 billion of the national health expenditures, faster than the 3.8% growth rate in 2018.[11] Some sources estimate that the percentage of spending on prescription drugs is actually closer to 15% of total spending, when accounting for non-retail drug sales as well as the gross profits of other parties in the drug supply chain, such as wholesalers, pharmacies, PBMs, providers, and payers.[12]

In part because of the federal dollars at stake, health care is the primary target of federal civil enforcement actions, including with respect to drug pricing and market access issues. In 2021, the federal government recovered more than $5.6 billion in settlements and judgments under the False Claims Act ("FCA"), which prohibits persons from making false claims (or causing false claims to be made) to the government – $5 billion related to health care cases, including those involving drug and medical device manufacturers, managed care providers, hospitals, pharmacies, hospice organizations, laboratories, and physicians.[13] The total recovery in 2020 was the second-largest amount on record in FCA history, and the largest since 2014.[14] In addition, 2020 was the 11th consecutive year in which civil health care fraud recoveries exceeded $2 billion.[15] Additionally, the federal government utilizes the Anti-Kickback Statute ("AKS") to combat activity that increases utilization and costs to federal programs, skews prescribing and other health care decisions, and creates an uneven competitor playing field.[16] Navigating this enforcement landscape requires a sophisticated understanding of the FCA, AKS, and government price reporting laws, as well as corresponding state laws.

The cost of prescription drugs

The high list price of prescription drugs in the U.S. is frequently discussed in the press and public discourse. Yet, the headlines often fail to capture both the types of drugs driving health care expenditures and the intricacies of the drug supply chain that create a significantly lower net price for a given drug product.

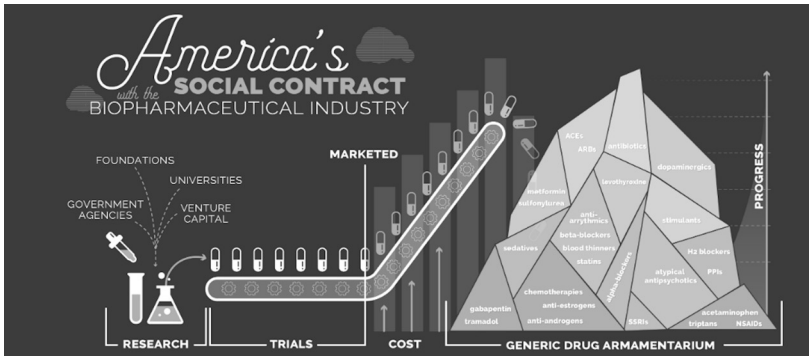
Branded versus generic drugs

Approximately 9 out of 10 prescriptions filled are for inexpensive generic drugs.[17] Prescription drug spending is primarily driven by the price of on-patent drugs. In general, after 10–15 years, these branded drugs lose patent protection, and inexpensive generic versions enter the market.

As illustrated in Figure 3, from Peter Kolchinsky's article entitled "American's Social Contract with the Biopharmaceutical Industry", the high price of branded drugs supports a "growing mountain" of highly utilized generic drugs.[18] Offering manufacturers higher prices for on-patent drugs for a limited period of time incentivizes innovation. The U.S. receives a return on its investment after the patent expires, at which point the drug rapidly declines in price. Payers encourage the utilization of generic drugs by implementing lower cost-sharing requirements.

See overleaf

Figure 3: America's social contract with the biopharmaceutical industry[19]



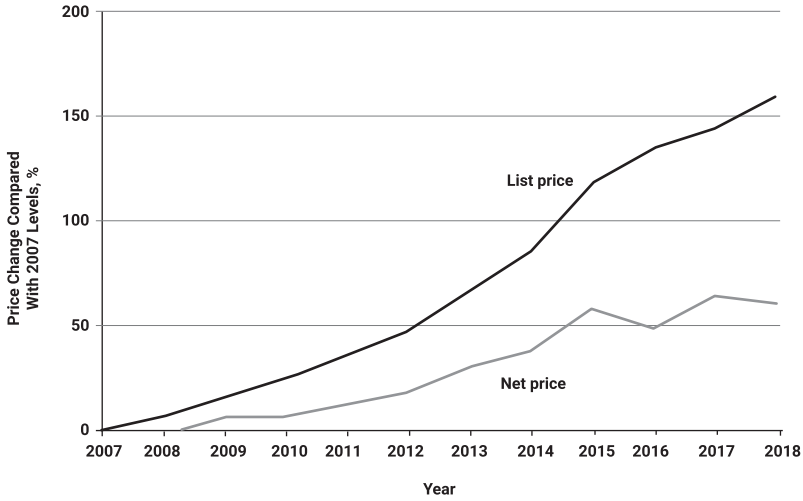
A small subset of branded drugs are known as "specialty drugs." Medicare defines specialty drugs as pharmaceuticals costing $670 or more per month,[20] and other payers look at factors beyond price, designating products as specialty drugs if they (1) are novel therapies, (2) require special handling, monitoring, or administration, or (3) are used to treat rare conditions.[21] Specialty drugs account for approximately 2% of prescriptions but over half of prescription drug spending.[22] Further, specialty share of net prescription drug spending increased from 27% in 2010 to 53% in 2020.[23] This trend is driven in large part by innovation – specialty drugs represented the largest proportion of new drug products launched during this time period – and also in part by patent expirations for traditional drug products.[24] In particular, cell and gene therapies represent the next frontier of specialty medications, with products such as chimeric antigen receptor T-cell ("CAR-T") therapy presenting tremendous promise to treat cancer on a highly personalized level. Many of these innovative treatments are priced – or are expected, once approved, to be priced – above $1 million for a course of treatment, but offer potential cures for otherwise fatal and/or debilitating conditions. Often, companion diagnostics and/or next generation sequencing tests are required as a prerequisite to accessing specialty drugs, and these tests have their own reimbursement and pricing dynamics.[25]

List price versus net price

Figure 4 illustrates that there is a significant gap between the list prices often cited in policy debates on drug pricing and the net prices actually reflecting the amount of money manufacturers receive.

See overleaf

Figure 4: List price *versus* net price[26]



Changes from 2007 to 2018 in list and net prices for branded products that were available in January 2007 and for which U.S. sales were reported by publicly traded companies. Net prices are net of all concessions made by manufacturers including rebates, coupon cards, 340B discounts, prompt pay discounts, return provisions, and any other deductions captured in the reporting of net sales.

The gap between list price and net price reflects various price concessions, such as discounts and rebates, associated with the numerous transactions throughout the U.S. drug supply chain, including among entities such as manufacturers, wholesalers, pharmacies, PBMs, and payers. According to the Pew Charitable Trust, manufacturer rebates grew from $39.7 billion in 2012 to $89.5 billion in 2016, significantly offsetting increases to drug list prices.[27] The prevalence of additional fees, such as administrative and service fees required by PBMs, may also impact pricing considerations.

Global comparisons

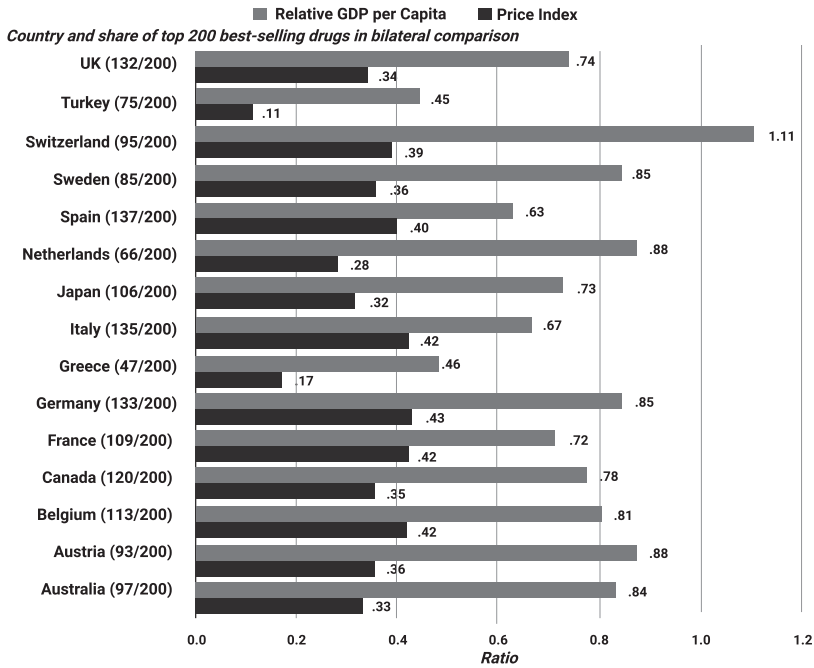
Health care spending in the U.S. outpaces international averages. In 2020, national health care expenditures generated 19.7% of GDP (in comparison to the Organisation for Economic Co-operation and Development ("OECD") average of 9.9%), totaling about $12,530 *per capita*.[28]

Prices for prescription drugs are significantly higher in the U.S. in comparison to other industrialized nations. Figure 5, reproduced from a report by the Council of Economic Advisers ("CEA"), shows the U.S. Price Index for 200 top-selling prescriptions, as well as relative GDP *per capita*. As the chart demonstrates, observed patented drug prices are far higher in the U.S. than can be explained by differences in *per capita* income alone. A price index of 0.34, for instance, indicates that prices in the United Kingdom are 34% of those in the U.S., even though the GDP in the United Kingdom is 74% of that in the U.S.

On the other hand, as demonstrated in the parentheticals along the y-axis, many of the 200 top-selling drugs are not available for sale in the countries of comparison. For example, in the United Kingdom, only 132 of the 200 drugs showed evidence of significant sales. Put another way, certain prescription drugs, such as some of the most innovative treatments for cancer, are more readily available in the U.S. than they are abroad. In its analysis, the

CEA states that "[t]he absence of significant sales volume for these drug products might be the result of delayed regulatory approval, a decision by a public insurance program not to cover a drug based on health technology assessment criteria, or other factors".[29] Numerous studies have demonstrated that restrictive coverage and reimbursement policies and price controls can impede development of innovative products.[30] As an example, research has shown that after Germany adopted more onerous price regulations in 1992, innovative research and development conducted in Germany subsequently dropped.[31]

Figure 5: Foreign-U.S. Price Index for 200 top-selling prescriptions and relative GDP *per capita* for selected nations, 2017[32]



SOURCES: Food and Drug Administration; IQVIA; OECD.

Pharmaceutical pricing and reimbursement

Marketing authorization

All drug products must be approved for use in the U.S. by the Food and Drug Administration ("FDA"), which is a government agency within the Department of Health and Human Services ("HHS"). FDA is charged with "protect[ing] the public health", including by ensuring that drugs are safe and effective, and "promot[ing] the public health" by efficiently reviewing and approving new drug products.[33] Currently, there are over 20,000 prescription drugs approved for marketing in the U.S., as well as 300 FDA-licensed biological products.[34]

FDA approves new drugs and new uses of approved drugs on the basis of safety and effectiveness. Innovative drug products are approved through New Drug Applications ("NDAs") and Biologics Licensing Applications ("BLAs").[35] Manufacturers must demonstrate

substantial evidence of effectiveness (or, for biologics, evidence that the product is "safe, pure, and potent") based on adequate and well-controlled clinical investigations.[36] FDA may also approve generic versions of an approved drug product as well as biological products that are biosimilar to a reference product.[37] Generic drug approval requires proof of bioequivalence, whereas a biosimilar must be highly similar to the reference product, with "no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product".[38] In 2021, FDA approved 63 new drugs and biological products, 93 first-time generic drugs, and four biosimilar products.[39]

FDA's timeline for reviewing NDAs and BLAs is generally set by a commitment letter issued by the Agency under the Prescription Drug User Fee Act of 1992 ("PDUFA"). Following criticism of the slow pace at which FDA approved new drugs during the HIV/AIDS crisis in the 1980s, Congress passed PDUFA in 1992 to authorize the collection of user fees from drug manufacturers in order to help fund FDA's drug approval process.[40] Congress reauthorizes PDUFA every five years, and reauthorization is forthcoming ahead of the expiration of PDUFA on September 30, 2022. In addition, parallel user fee programs now exist for generic drugs ("GDUFA") and biosimilars ("BsUFAs"). In FY 2021, 46% of FDA's budget was paid for by user fees, with the remaining 54% provided by federal budget authorization.[41] Performance goals under PDUFA stipulate that FDA aims to review and act on 90% of standard NDA and BLA submissions within 10 months of either filing (for new molecular entity ("NME") drug products and original BLAs) or receipt (for non-NME drug products).[42] Certain drug products may also be eligible for priority review, under which FDA aims to review and act on 90% of NDA and BLA submissions within six months of either filing or receipt.[43]

An NDA or BLA can receive priority review if it is for a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness.[44] In addition to priority review, other programs may be available to help expedite the development and review of drugs intended to address unmet medical need in the treatment of serious or life-threatening diseases or conditions, including breakthrough therapy designation, fast-track designation, and accelerated approval.[45]

In addition to approving new drugs, FDA also grants exclusive marketing rights to drugs approved under certain criteria. New chemical entities, meaning drugs that contain no active moiety that has been approved by FDA, benefit from five years of marketing exclusivity, running from the time of NDA approval.[46] During that time, FDA cannot accept for review any NDA or abbreviated NDA ("ANDA") or a drug containing the same active moiety.[47] FDA offers 12 years of exclusivity for biologics, seven years for orphan drugs (drugs designated and approved to treat diseases or conditions affecting fewer than 200,000 in the U.S., or more than 200,000 with no hope of recovering costs), three years for applications or supplements containing new clinical investigations, and six additional months of market protection where the sponsor has conducted and submitted pediatric studies.[48] Other incentives are also available, such as priority review vouchers for drugs treating neglected tropical diseases, rare pediatric diseases, and medical countermeasures.[49]

Unlike regulators in many other countries, FDA does not consider price or cost-effectiveness in approving prescription drug products through the use of health technology assessment ("HTA") bodies or otherwise regulate the prices charged by manufacturers or reimbursement offered by payers. As described in further detail below, however, both government and private payers view FDA approval as a precondition for reimbursement.

Coverage and reimbursement

Whether a drug product is covered, and at what price, is determined by each payer's

coverage, coding, and payment criteria. This section provides key terminology applicable to coverage and reimbursement,[50] followed by a summary of criteria for reimbursement under the two largest government-sponsored plans, Medicare and Medicaid, as well as the 340B Program. This section also includes considerations for coverage and reimbursement under private plans.

Key terminology

Actual Acquisition Cost ("AAC"). A state Medicaid program's determination of a pharmacy's actual price paid to acquire a drug product marketed or sold by a manufacturer.[51]

Average Manufacturer Price ("AMP"). The average price paid to the manufacturer for a drug in the U.S. by (1) wholesalers for drugs distributed to retail community pharmacies, and (2) retail community pharmacies that purchase the drug directly from the manufacturer.[52]

Average Sales Price ("ASP"). The average price of a manufacturer's sales of a drug (by National Drug Code) to all purchasers in the U.S., as calculated by sales divided by the total units of the drug sold by the manufacturer in the same quarter.[53]

Average Wholesale Price ("AWP"). The list price of a drug from a wholesaler to a pharmacy, as calculated and published by certain price reporting compendia.[54]

Best Price. The lowest available price offered by the manufacturer to any wholesaler, retailer, or provider, excluding certain government programs.[55]

Wholesale Acquisition Cost ("WAC"). The list price of a drug from a manufacturer to wholesalers or direct purchasers, not including prompt pay or other discounts, rebates or reductions in price.[56]

Government-sponsored plans and programs

A. **Medicare**

Medicare was established in 1965 under Title XVIII of the Social Security Act of 1965 ("SSA") as a federally funded program to provide health insurance to individuals aged 65 and older.[57] It has since been expanded to cover individuals with disabilities or end-stage renal disease ("ESRD"). CMS administers the Medicare program, along with Medicaid and certain other federal health care programs.

i. Benefit designs

Medicare benefits are defined by statute, and Medicare provides coverage only for an item or service that falls within the statutorily identified benefit categories. In addition, the Medicare statute expressly excludes from coverage certain items or services, such as cosmetic surgery and some dental services. For a drug product to be covered by Medicare, it must, among other things, be "reasonable and necessary for the diagnosis or treatment of an illness or injury or to improve the functioning of a malformed body member".[58] The Medicare program is divided into four parts that offer different benefits for beneficiaries:

- Part A provides hospital insurance that covers inpatient hospital services, as well as post-hospital skilled nursing facility services, hospice care, and some home health services. Inpatient hospital services include drug products and biologics.[59] Individuals aged 65 and older generally qualify for premium-free Part A benefits based on payroll taxes they or their spouses paid. Individuals under age 65 who have received disability benefits for at least 24 months also qualify for premium-free Part A benefits. Part A benefits are managed by Medicare Administrative Contractors ("MACs"), which are private health care insurers awarded geographic jurisdictions to process certain Medicare claims.[60] MACs make coverage determination on a

case-by-case basis or as local coverage determinations ("LCDs") or pursuant to national coverage determinations ("NCDs").[61]

- Part B provides supplemental medical insurance for a range of outpatient services, including physicians' services, laboratory services, durable medical equipment ("DME"), and other medical services.[62] Part B also provides coverage of certain items and supplies, such as outpatient drug products that are not usually self-administered and are furnished incident to a physician's services.[63] All individuals entitled to Part A may voluntarily enroll and obtain Part B benefits for a monthly premium.[64] Like Part A benefits, Part B benefits are managed by MACs, which determine coverage on a case-by-case basis or based on LCDs or pursuant to NCDs.[65] Parts A and B, together, constitute "original Medicare".[66]
- Part C Medicare Advantage ("MA"), formerly known as Medicare +Choice, provides an alternative method for beneficiaries to receive benefits. Instead of receiving benefits separately through Part A and Part B, beneficiaries may choose to enroll in an MA plan offering combined Part A and Part B benefits.[67] MA plans are administered by private health plans, such as health maintenance organizations ("HMOs"), preferred provider organizations ("PPOs"), private fee-for-service ("PFFS") plans, and special needs plans ("SNPs"). These private plans contract with CMS to provide all the required Part A and Part B benefits through a managed care system.[68] Plans may also offer alternative cost-sharing arrangements for beneficiaries or coverage for additional benefits not covered under original Medicare, such as over-the-counter ("OTC") drugs, vision care, or dental services.[69] All MA plans, except PFFS plans, must offer options that include coverage for prescription drugs ("MA-PDs").[70] MA-PDs generally must comply with Part D requirements, as discussed below.
- Part D was established by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") and first implemented in 2006. Part D offers voluntary prescription drug coverage for beneficiaries entitled to Part A benefits or enrolled in Part B. Beneficiaries with original Medicare can enroll in a stand-alone prescription drug plan ("PDP") that is administered by a private health plan.[71] Part D plan sponsors create formularies identifying the prescription drugs that are covered by their plans. Formularies must meet federally specified criteria, including coverage of all therapeutic categories and classes and providing at least two drugs in each category or class.[72] Part D plans must be reviewed and approved by CMS.[73]

ii. Coverage and reimbursement methodology

As a preliminary matter, drug products generally must be approved by FDA in order to be reimbursed by Medicare. Parts A and B, however, cover only items or services that are "reasonable and necessary for the diagnosis or treatment of an illness or injury or to improve the functioning of a malformed body member".[74] Thus, drug products also must be considered "reasonable and necessary" based on available clinical and scientific evidence, which is a different standard from FDA approval. In addition, Part D covers only outpatient prescription drug products that are FDA approved and used for a medically accepted indication.[75]

Coverage determinations for drug products vary depending on which Part of Medicare is reimbursing. With respect to Medicare Parts A and B, most coverage determinations are made by MACs on a case-by-case basis or through LCDs to determine whether a given product will be covered in the MAC's jurisdiction. CMS

also can issue NCDs to determine coverage of a drug product nationwide; while NCDs for drugs are rare, recent notable examples include the NCD for CAR-T therapies and the NCD with coverage with evidence development for monoclonal antibodies that target amyloid (or plaque) for the treatment of Alzheimer's disease.[76] For LCDs, MACs typically review new drug products upon submission of an LCD request, which triggers a 60-day review period to determine whether the request is complete, and then a lengthier review to evaluate the request itself, invite and incorporate public comment, and ultimately issue a final determination.[77]

Under Part D, the private plan sponsors administering the PDP and MA-PD benefits determine which prescription drug products are covered. The plan sponsors develop formularies to identify which prescription drug products are covered, subject to the requirements above. Formularies usually include "tiers" setting forth different beneficiary cost-sharing requirements.[78] Part D formularies must be developed and reviewed by a pharmacy and therapeutics ("P&T") committee, which must "make a reasonable effort" to review new drug products within 90 days and make coverage determinations within 180 days of a drug's introduction to the market.[79] CMS reviews formularies to ensure that they are consistent with federal requirements related to formulary design. A plan must cover at least two drugs for a particular therapeutic class,[80] and must cover "substantially all" immunosuppressant (for prophylaxis of organ transplant rejection), antidepressants, antipsychotics, anticonvulsants, antiretrovirals, and antineoplastics.[81]

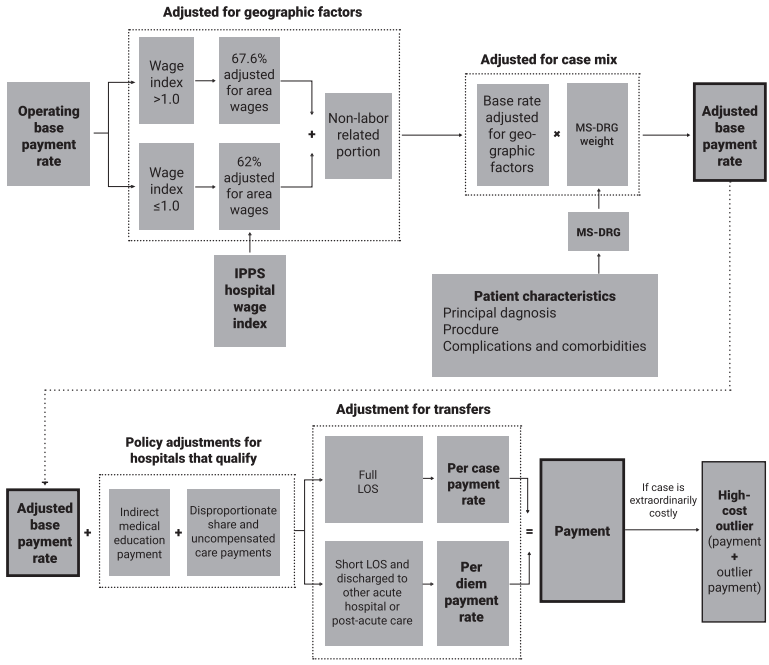
Part A reimbursement

Reimbursement for most acute care hospital services under Part A is determined using the inpatient prospective payment system ("IPPS") based on diagnosis-related groups ("DRGs"). The IPPS was established by Congress through the Social Security Amendments of 1983.[82] Reimbursement under Part A is intended to cover all the services and supplies provided during the beneficiary's spell of illness, including any drug products provided to the beneficiary; hospitals are statutorily prohibited from billing for items and services separately, or "unbundling" items and services.[83]

The IPPS formula contains two basic components. First, a base payment amount is prospectively determined by CMS to cover the operating and capital expenses per discharge, adjusted by a wage index for the geographic area in which the hospital is located.[84] Second, a weighting factor is associated with the DRG to which the beneficiary is assigned, to account for the resources required to treat the beneficiary.[85] The base payment amount, adjusted by the wage index, is multiplied by the weight of the beneficiary's DRG to determine the reimbursement payment amount. Medicare may also provide add-on payments, on top of the adjusted base payment, to cover costs associated with extraordinary treatment cases ("outliers"), teaching hospitals, or qualified new technologies. Disproportionate share hospitals ("DSHs") that treat a certain volume of low-income patients receive additional payments for operating and capital expenses.[86] Additionally, Medicare has established several quality incentive programs under which hospitals may receive incentive payments or penalties associated with quality of care criteria set by CMS.[87]

Certain hospitals, or hospital units, are exempt from the IPPS and receive reimbursement based on alternative methodologies. These include psychiatric hospitals or units, rehabilitation hospitals or units, children's hospitals, and long-term care hospitals.[88]

Figure 6: Acute inpatient prospective payment system for Fiscal Year 2022[89]



Note: MS-DRG (Medicare severity diagnosis related group), LOS (length of stay). Capital payments are determined by a similar system. Additional payments are also made for certain rural hospitals. Hospitals may receive penalties or additional payments based on their performance on quality standards.

Part B reimbursement

Medicare reimburses certain drug products under Part B when they are administered "incident to" a physician's services, generally in the physician's office or other outpatient setting.[90] Part B drugs include, for example, drugs that are infused or injected. These drugs are reimbursed under the "buy and bill" model, through which providers first purchase drugs and then submit claims for reimbursement after the drugs have been administered to a beneficiary. In order to obtain reimbursement for Medicare Part B drugs, providers must submit claims to MACs using Healthcare Common Procedure Coding Systems ("HCPCS") codes.[91]

The current reimbursement methodology for most Part B drugs was established by the MMA.[92] Under this methodology, reimbursement payments for Part B drugs are generally calculated based on the ASP, which the manufacturer reports to CMS.[93] A drug's ASP is calculated by dividing the manufacturer's sales of the drug to all purchasers in the U.S. in a specific quarter (excluding nominal sales to certain entities and sales that are exempt from the determination of Medicaid best price) by the number of units of the drug sold by the manufacturer in the same quarter.[94]

Manufacturers report ASP on a quarterly basis. Whereas ASP reporting historically has been required only for those manufacturers with Medicaid rebate agreements, as of January 1, 2022, manufacturers that do not have a rebate agreement with CMS are required to report ASP data for items, services, and products payable under Medicare Part B as drug products.[95] Reimbursement rates are updated quarterly; however, the rates are calculated using the reported ASP from two quarters ago.[96]

Reimbursement for Part B drugs administered in the physician office setting is statutorily set at 106% of ASP, referred to as "ASP+6".[97] Beneficiaries are generally responsible for 20% of the cost of drug products under Part B.[98] ASP+6 is intended to account for variability in provider acquisition costs and to compensate providers for the additional costs associated with the complexity of Part B drugs, many of which are used to treat serious illnesses such as cancer, cerebral palsy, and multiple sclerosis. Specific Part B drugs, including certain preventative vaccines, compounded drugs, and certain radiopharmaceuticals, are reimbursed based on the product's AWP, rather than at ASP+6.[99] Payments for newly launched Part B drugs are based on a percentage of WAC until ASP data are available (typically for the first two quarters the drug product is on the market), since ASP data are often not available when a drug product is brought to market.[100] In 2019, the payment rate for new drugs was lowered from 106% of WAC to 103% of WAC.[101]

In certain settings of care, reimbursement for Part B drugs is included, or "bundled", with the payment for other services. For example, payments for certain drugs administered in hospital outpatient departments and ambulatory surgical centers are bundled with the payments for services under the hospital outpatient prospective payment system ("OPPS").[102] Other drug products, such as drugs with pass-through status, are reimbursed separately under OPPS. Reimbursement rates for such drugs vary from year to year and are currently set at ASP+6 for most drugs and ASP minus 22.5% for most drugs acquired through the federal 340B Program, discussed below.[103]

Part C reimbursement

MA plans contract with CMS to provide all required Part A and Part B items and services to Medicare beneficiaries in exchange for a monthly capitated payment. MA contracts are awarded based on a competitive bidding process. Reimbursement payments are then calculated by comparing the plan's bid, which establishes the plan's estimated costs of providing Part A and Part B services to the average beneficiary to the benchmark plan. If the plan's bid is lower than the benchmark, the reimbursement payment equals the bid amount, plus a rebate based on the difference between the bid and the benchmark that is passed on to the beneficiaries. However, if the bid is equal to or greater than the benchmark, the benchmark will be the reimbursement payment, and beneficiaries are required to pay an additional premium based on the difference between the bid and the benchmark.[104]

For MA-PD plans offering prescription drug coverage, a separate Part D bid must be submitted to CMS. Reimbursement for the prescription drug part of the MA plan is then calculated separately, in the same manner as stand-alone PDPs (discussed below).[105]

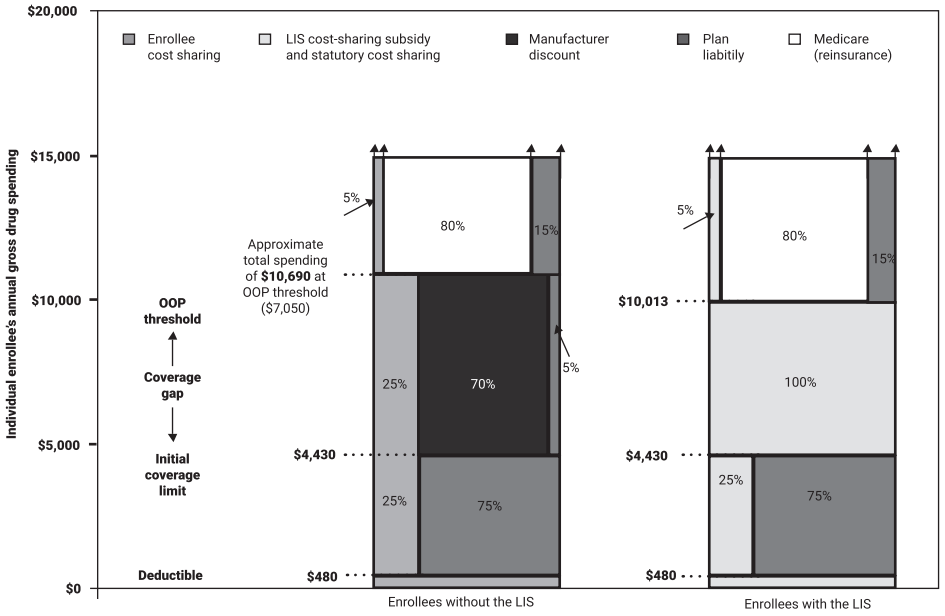
Part D reimbursement

Under Part D, stand-alone PDPs must provide standard prescription drug coverage, as set forth by statute, or alternative coverage that provides actuarially equivalent benefits.[106] In 2022, the standard benefit includes a $480 deductible and 25% coinsurance for the cost for both brand-name and generic drug products between $480 and $4,430. Beneficiaries then enter the coverage gap, also referred to as the "doughnut hole", until they reach the catastrophic limit and out-of-pocket threshold of $7,050. After reaching the catastrophic limit, beneficiaries pay the higher of either a 5% coinsurance or a set amount per prescription.[107] Under Part D as it was originally implemented in 2006, beneficiaries were responsible for all drug costs incurred while they were in the coverage gap. However, provisions of the Patient Protection and Affordable Care Act (often shortened to the Affordable Care Act or "ACA") slowly reduced cost-sharing requirements during the doughnut hole, including by phasing in larger Medicare subsidies and requiring manufacturers to provide discounts for brand-name drug products

purchased by beneficiaries in the coverage gap.[108] As of 2020, from the perspective of the beneficiary, the doughnut hole is closed, meaning beneficiaries are responsible for only the 25% coinsurance until they reach the out-of-pocket threshold.[109] Once beneficiaries surpass the out-of-pocket threshold, they enter the catastrophic coverage phase and must pay the lesser of either 5% coinsurance or a fixed amount for prescription drug products.[110]

Different cost-sharing obligations apply for qualifying beneficiaries who receive low-income subsidies ("LIS") under Part D, for which the federal government pays in full or in part the drug cost-sharing expenses.[111] Full LIS beneficiaries have no deductible but do have subsidized coinsurance payments in the initial coverage (25%), coverage gap (25%), and catastrophic coverage (5%) phases, with a copayments; partial LIS beneficiaries have a deductible plus a coinsurance of 15% through the coverage gap phase and a copayment in the catastrophic coverage phase.[112]

Figure 7: Part D 2022 standard defined benefit and LIS benefit structures[113]



Note: LIS (low-income subsidy), OOP (out of pocket). For beneficiaries without the LIS (left bar), the coverage gap is depicted as it would apply to brand-name drugs, which are eligible for a 70% manufacturer's discount in the coverage gap. There is no discount for generic prescriptions, and thus cost sharing in the coverage gap is 25% and plans are responsible for 75%. Because of this difference, total covered drug spending at the OOP threshold depends on the mix of brand and generic prescriptions each individual fills while in the coverage gap. The dollar amount shown ($10,690) was estimated by CMS for an individual with an average mix of drugs who does not receive Part D's LIS and has no other supplemental coverage. The bar depicting LIS enrollees (right) reflects full rather than partial LIS coverage. LIS enrollees do not receive brand discounts from manufacturers. Beneficiaries who receive full Medicaid and Medicare benefits

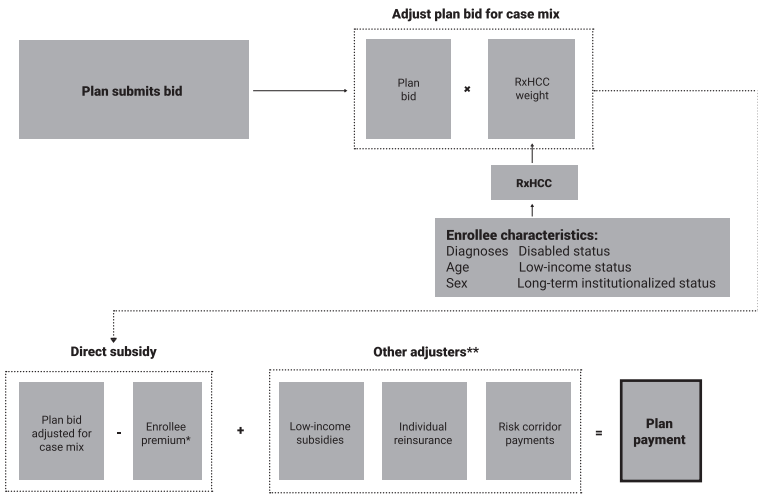
and have incomes less than or equal to 100% of the federal poverty level ("FPL") pay no deductible, copayments of no more than $1.35 per generic prescription, $4.00 per prescription for other drugs, and no copayments above the OOP threshold. Other beneficiaries who receive full Medicaid and Medicare benefits pay no deductible, copayments of no more than $3.95 per generic prescription, $9.85 per prescription for other drugs, and no copayments above the OOP threshold. Institutionalized enrollees pay no cost sharing. Beneficiaries who receive partial LIS assistance pay a deductible of $99.00, 15% coinsurance up to the OOP threshold, and thereafter copayments of $3.95 per generic prescription and $9.85 per prescription for other drugs.

Source: MedPAC depiction of Part D benefit structure for 2022.

Part D reimbursement payments made to PDPs and MA-PDs are based on a competitive bidding process. Plan sponsors determine their bids based on the expected costs of providing coverage for the average Medicare beneficiary. CMS provides monthly capitated payments to plans to subsidize the standard benefit coverage.[114] As noted above, CMS also pays additional subsidies for LIS beneficiaries and reinsurance subsidies to cover the costs of beneficiaries with high prescription drug expenses.

Unlike reimbursement under Medicare Part A and Part B, the federal government does not play a role in determining the calculation for drug product reimbursement under Part D. Instead, plan sponsors usually contract with PBMs to negotiate prices with manufacturers. Plans also establish a network of pharmacies to provide access to covered drug products for its beneficiaries.[115] The Medicare statute prohibits the federal government from interfering with Part D price negotiations or establishing a required formulary or reimbursement formula for Part D drug products.[116]

Figure 8: Part D payment system[117]



Note: RxHCC (prescription drug hierarchical condition category). The RxHCC is the model that estimates the enrollee risk adjuster. CMS uses five separate sets of model coefficients for: long-term institutionalized enrollees; aged low-income enrollees; aged non-low-income enrollees; disabled low-income enrollees; and disabled non-low-income enrollees.

** Figure 8 outlines the process for calculating enrollee premiums.*

*** Plans receive interim prospective payments for individuals' reinsurance and LIS that are later reconciled with CMS.*

B. Medicaid

Medicaid was established by the SSA to provide health care services to low-income individuals.[118] The program is funded jointly by federal and state governments. States are not required to participate in Medicaid; however, all 50 states, Washington, D.C., and the U.S. territories have chosen to participate. The federal Medicaid statute establishes federal requirements that states must satisfy in order to receive matching federal funds. However, the statute also provides flexibility for states to design their programs within the federal guidelines.[119]

In order to receive Medicaid benefits, individuals must qualify through an eligibility pathway that provides coverage to identified populations. Some pathways are mandated by federal law, while others are optional pathways that states may choose to offer. States may also apply for a Medicaid waiver in order to offer coverage to populations beyond the mandatory and optional pathways. The federal Medicaid statute defines the categories of individuals who are covered by a certain pathway ("categorical eligibility") and whether there are any financial requirements ("financial eligibility"), as well as the extent to which a state can alter or adjust the pathway's requirements.[120]

i. Benefit designs

Medicaid coverage includes a range of benefit options, including primary care, preventative care, and long-term care services and supports. Medicaid beneficiaries may receive benefits through a fee-for-service ("FFS") system or a managed care system, depending on which systems are offered by the state. Through the FFS system, states provide reimbursement to health care providers for each service they provide to beneficiaries. Through the managed care system, states pay managed care organizations ("MCOs") a monthly capitated fee to provide benefits to eligible individuals.[121]

An individual's benefits vary based on the eligibility pathway through which he or she obtains coverage. State programs may offer either traditional Medicaid benefits, which include a range of required and optional benefits specified by federal law, or alternative benefit plans ("ABPs"), which are based on a coverage benchmark but must include the essential health benefits ("EHBs") that private health plans are generally required to provide. States may also apply for a Medicaid waiver to provide additional services.[122] Under the traditional Medicaid benefit framework, prescription drug coverage is an optional benefit, but all states have chosen to offer it; for ABPs, prescription drug coverage is a mandatory benefit.[123] Further, some state Medicaid programs also provide coverage for OTC drug products.[124]

Individuals who are eligible for both full Medicaid benefits and Medicare, known as "dual eligibles", generally must obtain prescription drug coverage through a Medicare Part D plan. State Medicaid agencies are statutorily prohibited from providing reimbursement for drug products covered by Part D for dual eligible; however, agencies may provide reimbursement for drug products that are expressly excluded from the definition of a covered Part D drug.[125]

ii. Coverage and reimbursement methodology

Pursuant to the Medicaid Drug Rebate Program ("MDRP"),[126] state Medicaid programs must maintain an "open formulary" covering all drugs by a participating manufacturer.[127] In exchange, manufacturers agree to make rebate payments intended to ensure that Medicaid pays the "best price" for drug products.[128] Many states also have developed preferred drug lists ("PDLs"), which include drugs for which manufacturers offer supplemental rebates beyond those offered by the MDRP. Providers are encouraged to prescribe drugs on the state PDL to Medicaid

beneficiaries; the drugs on the PDL are generally subject to fewer utilization management controls. Additionally, the federal Medicaid statute allows state programs to exclude certain drugs, classes of drugs, or drug uses from coverage.[129]

State Medicaid programs usually reimburse community retail pharmacies for drug products dispensed to Medicaid beneficiaries. In addition, some states may require Medicaid beneficiaries to pay a nominal copayment for outpatient prescription drug products.[130]

FFS Medicaid reimbursement payments to pharmacies are generally based on the drug product's ingredient cost and the pharmacist's dispensing fee. In 2016, CMS issued a final rule requiring states to use the AAC to determine ingredient cost.[131] However, federal regulations permit states to choose how they calculate AAC by using either a survey of pharmacy providers, the AMP, or the National Average Drug Acquisition Cost ("NADAC").[132] The drug's ingredient cost is combined with a professional dispensing fee, which is usually a fixed amount intended to cover the pharmacy's costs for obtaining, storing, and dispensing the drug.[133]

Medicaid managed care plans also reimburse pharmacies for drug products dispensed to beneficiaries. Like payments made by FFS Medicaid, managed care reimbursement rates are based on the drug's ingredient costs and dispensing fees. To calculate ingredient costs, MCOs are not required to use the AAC but must make payments sufficient to ensure appropriate access for their beneficiaries.[134] MCOs negotiate reimbursement terms with pharmacies rather than creating a generally applicable payment formula. They also may negotiate their own rebates and other discounts from manufacturers.[135]

Many states contract with PBMs, which serve as intermediaries between the state Medicaid agencies, pharmacies, manufacturers, and beneficiaries. States may use PBMs for Medicaid programs administered on an FFS basis or through a managed care system to perform multiple administrative and financial functions. PBMs working on behalf of MCOs may negotiate drug prices with pharmacies; conversely, PBMs working with Medicaid programs must comply with federal and state requirements for drug reimbursement.[136] Concerns regarding the lack of transparency for PBMs have led to growing efforts to regulate PBMs at the state level. For example, some states require that PBMs adhere to certain disclosure requirements related to rebates that the PBM receives from manufacturers that are not passed through to the health plans.[137] In addition, several states have opened investigations into the practices used by PBMs in the delivery of Medicaid benefits.[138] For example, Ohio's Attorney General has filed several lawsuits against PBMs since 2019, challenging the rise in PBMs' spread pricing profits under the state's Medicaid managed care program.[139]

To control the cost of prescription drugs, federal and state governments have implemented policies to create certain payment limitations for Medicaid reimbursements. The federal upper limit ("FUL") is a payment limitation that caps the reimbursement payment for ingredient costs of certain multiple source drugs.[140] Currently, CMS has set the FUL at 175% of the weighted average of the most recently reported AMP for the specific form and strength of a drug.[141] In addition, most states have created a maximum allowable cost ("MAC") program to limit reimbursements for certain multiple source drugs. State MAC programs operate similarly to the FUL cap; however, states have discretion to decide which drugs are included in the program and how the reimbursement limitation for those drugs is calculated. As of

2014, 45 states had established MAC programs.[142] Finally, for single source drugs and drugs not subject to FUL or MAC limitations, reimbursement – in the aggregate – may be determined by the lower of either (1) the AAC and dispensing fee, or (2) the providers' usual and customary charges to the general public.[143]

Pursuant to the MDRP, as discussed above, a drug product is covered by Medicaid only if the manufacturer enters into a Medicaid rebate agreement.[144] The agreement requires the manufacturer to provide a rebate to the state's Medicaid agency, which is then shared between the federal and state governments in order to reduce federal and state expenditures. For single source and innovator multiple source drugs, Medicaid's basic rebate formula requires a payment in the amount of the greater of either the difference between a drug's quarterly AMP and the best price for the same period, or a flat percentage (23.1%) of the drug's quarterly AMP.[145] Drug manufacturers owe an additional rebate when their AMPs for individual products increased faster than inflation. For other drug products, separate rebate structures would apply, as demonstrated in Figure 9.

Rebates for new formulations of brand name drug products, referred to as "line extensions," are calculated using a separate rebate formula. On December 31, 2020, CMS published a final rule updating the MDRP regulations in part to expand the universe of drugs that would be considered line extensions.[146] According to the 2020 final rule, the alternative rebate formula must be applied to the line extension only if the manufacturer of the line extension also manufactures or has a "corporate relationship" with the manufacturer of the original drug.

Figure 9: Medicaid drug rebate formulas[147]

Drug Category	Basic Rebate	Additional Rebate
Single Source	The greater of either 23.1% of AMP per unit or AMP minus best price per unit	Required when prices rise faster than the inflation rates – difference between the products' per unit current AMP and the base period AMP adjusted by CPI-U[148] for each quarter since launch
Innovator Multiple Source Drugs	The greater of either 23.1% of AMP or AMP minus best price per unit	Required when prices rise faster than the inflation rates – difference between the products' per unit current AMP and the base period AMP adjusted by CPI-U for each quarter since launch
Line Extension Products	The greater of (1) the basic and additional rebate for the new drug, or (2) the product of the line extension drug's AMP and the highest additional rebate for any strength of the original brand drug and the number of units of each dosage form and strength of the line extension drug	
Blood Clotting Factors	The greater of 17.1% of AMP per unit or AMP minus best price per unit	Required when prices rise faster than the inflation rates – difference between the products' per unit current AMP and the base period AMP adjusted by CPI-U for each quarter since launch
FDA Approved Pediatric Indication	The greater of 17.1% of AMP per unit or AMP minus best price per unit	Required when prices rise faster than the inflation rates – difference between the products' per unit current AMP and the base period AMP adjusted by CPI-U for each quarter since launch
Non-Innovator Multiple Source and Other Drugs	13% of AMP	Required when prices rise faster than the inflation rates – difference between the products' per unit current AMP and the base period AMP adjusted by CPI-U for each quarter since launch

Source: Congressional Research Service ("CRS") review of the SSA §1927. Payment for Covered Outpatient Drugs, and 42 Code of Federal Regulations ("CFR") § 447.502.

C. 340B Drug Pricing Program

The federal 340B Program requires manufacturers to provide outpatient prescription drugs to certain providers that serve low-income and uninsured individuals (frequently referred to as "safety net providers").[149] Established in 1992, the 340B Program was conceived to address an unintended consequence of the MDRP – the requirement to report the best price resulted in manufacturers no longer offering voluntary discounts to safety net providers.[150] Under the 340B Program, any manufacturer that participates in the MDRP must: (1) offer the 340B price if the drug is made available to any other purchaser at any price; (2) to covered entities (defined by Section 340B of the Public Health Service Act to include federally qualified health centers, various disease-specific programs, and publicly owned hospitals treating a disproportionate number of low-income patients); (3) cover outpatient drugs (defined by statute to include all outpatient drugs, including infusion therapies, provided they are not associated with an inpatient stay); and (4) set the 340B price at no more than a statutorily defined ceiling (the "ceiling price").[151]

The ceiling price is calculated on a quarterly basis using MDRP figures (AMP minus the Unit Rebate Amount ("URA")) from two quarters prior, except that 340B pricing is estimated for new drugs until the MDRP figures become available. Manufacturers may voluntarily offer lower "sub-ceiling" pricing to covered entities. After purchasing the drug at the ceiling price, the covered entity generally seeks reimbursement from the patient's insurance (commercial or government) or potentially the patient. The statute prohibits covered entities from obtaining duplicate discounts under 340B and MDRP, and bans them from diverting discounted drugs to anyone but their own patients. The mandatory discounts required under the 340B Program are exempt from best price (and related) calculations. Consequently, critiques of the program include that discounts are sometimes not passed onto the uninsured or underinsured patients and covered entities do not use the proceeds from the difference between the 340B price and the reimbursed amount to provide charity care.[152]

In 2010, the ACA expanded 340B eligibility to include additional categories of hospitals, and draft guidance from the Health Resources and Services Administration ("HRSA") removed the restriction on 340B entities' use of only one contract pharmacy, leading to growth in the number of 340B prescriptions.[153] In addition, hospital acquisition of oncology practices has driven increased 340B profitability for hospitals.[154] 340B spending has increased significantly in recent years, rising from $5.3 billion in 2010 to $24.3 billion in 2018.[155]

In 2018, HHS reduced Medicare Part B reimbursement rates for certain drugs acquired under the 340B Program from ASP+6 to ASP minus 22.5%, so as to "better, and more appropriately, reflect the resources and acquisition costs that these hospitals incur".[156] In litigation challenging this change in reimbursement, a U.S. District Court ruled that HHS exceeded its statutory authority by reducing the reimbursement rate in this manner.[157] In 2020, a U.S. Court of Appeals reversed the District Court's decision and determined that HHS had reasonably interpreted the Medicare statute and acted within its authority in implementing the rate cut of ASP minus 22.5% for drugs purchased under the 340B Program.[158] In February 2021, the American Hospital Association ("AHA"), the Association of American Medical Colleges ("AAMC"), and America's Essential Hospitals ("AEH") asked the U.S. Supreme Court to review the case. The petition for review was granted on July 2, 2021, and the Court heard oral arguments on the case in November 2021. As of April 2022, the Court has not issued a decision.[159]

In 2020, several manufacturers sought to prevent duplicate discounts and ineligible rebates in the 340B Program by limiting the distribution of 340B covered outpatient drugs via contract pharmacies. The 340B statute does not reference contract pharmacies; however, HRSA guidance in 2010 suggested that covered entities may create ship-to arrangements with an unlimited number of contract pharmacies.[160] In response to the manufacturers' limited distribution approach, HRSA sent individual manufacturers letters stating that their new contract pharmacy policies violate the 340B statute and that any overcharges must be refunded to impacted entities.[161] In several cases filed by the manufacturers that received the letters, U.S. District Courts have taken differing approaches as to whether HRSA has the authority to issue the letters and whether the manufacturers' actions related to the distribution of 340B covered outpatient drugs were permissible.[162] As of April 2022, multiple notices of appeal have been filed in several U.S. Courts of Appeal.

D. Private plans

Approximately two-thirds of Americans are covered by private insurance. The vast majority of those with private insurance have employment-based coverage – in 2020, 177.2 million Americans had coverage through an employer.[163] The ACA requires large employers to provide full-time employees and their dependents with coverage, and plans must meet minimum standards for affordability and coverage.[164] Employers generally pay most of the insurance premium on behalf of employees and their dependents, while employees are responsible for the remainder of the premium and cost-sharing requirements. On average, employers pay 82% of the premium for single coverage and 71% for family coverage.[165] Americans can also purchase insurance directly through state-based and multi-state Affordable Health Insurance Exchanges (also known as "Health Insurance Marketplaces"), where subsidies are available to individuals with incomes between 100% and 400% of the FPL.[166] Additionally, individual and group plans are also available for purchase outside of the Health Insurance Marketplaces.[167]

Private plans typically include medical and pharmacy benefits. Drugs used with DME are often covered under the pharmacy benefit. Physician-administered drugs, regardless of formulation, are typically covered and paid under the medical benefit. FDA approval is typically a prerequisite for coverage; however, private plans have greater flexibility than public plans in defining the benefit category and placement of drugs on formularies, as well as adopting utilization controls, as discussed below.

Medicare rates frequently serve as a floor for payments under private plans. However, unlike Medicare's Part A and Part B benefits, private payers can and do negotiate prices and payments, often through negotiated aggregate rebates with drug manufacturers facilitated by PBMs. Drug payment rates vary depending on contracts with providers, manufacturers, vendors, and employers. Private payers often consider cost or cost-effectiveness in the coverage process, with many utilizing complex formularies to determine patient cost-sharing responsibilities, as discussed below.

Additional issues that affect pricing and reimbursement

Other parties in the drug supply chain

Understanding the pharmaceutical supply chain is key to understanding the cost of prescription drugs in the U.S., particularly in the private market. Manufacturers rarely receive the WAC or list price set by manufacturers because products are frequently discounted throughout the distribution system. These discounts flow through wholesale distributors, pharmacies, payers and PBMs, and are often paid retrospectively by the manufacturer in the form of rebates. In addition to discounts, manufacturers also pay separate fees for various services provided by supply chain entities, including wholesalers, PBMs, and group purchasing organizations ("GPOs").

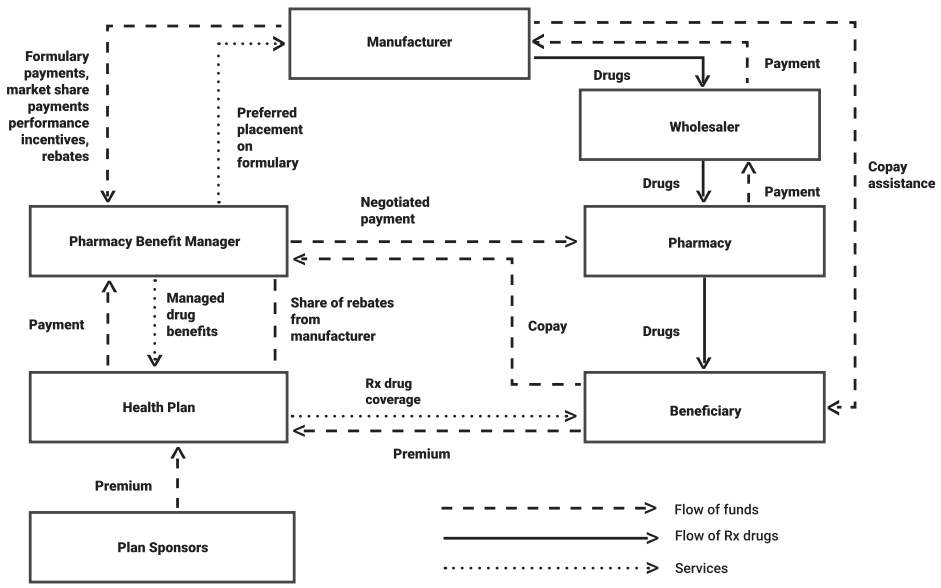
Wholesale distributors buy drugs from manufacturers and distribute them to pharmacies, hospitals, and other medical facilities. Pharmacies negotiate with wholesalers to purchase prescription drugs for their inventory, and, in turn, wholesalers negotiate with manufacturers to obtain drugs to distribute to pharmacies and other purchasers. Wholesalers also facilitate charge-backs for manufacturers to effectuate negotiated prices for their customers.

PBMs represent payers and employers in the selection, purchase, and distribution of prescription drug benefits, and often serve as a broker, without fiduciary obligations, between individual employers, payers, drug manufacturers, and pharmacies.[168] PBMs play several roles throughout the supply chain. These include:

- **Developing and maintaining prescription drug formularies for insurance plans.** PBMs maintain a national formulary, as well as custom client formularies, to provide tiered coverage for branded and generic prescription drugs.
- **Negotiating discounts from manufacturers.** PBMs negotiate discounts from manufacturers on behalf of insurers, in exchange for preferred formulary placement. Discounts generally come in the form of rebates. PBMs retain these rebates and pass along some portion of the manufacturer price concession under a blended effective rate for an employer's or plan's branded drug spend. Rebate agreements between PBMs and manufacturers often contain price protection provisions that require the manufacturer to pay additional concessions to the payer or PBM in the form of a penalty if the list price of the product increases above a predefined threshold year over year, on a cumulative multi-year basis, or both. Some larger payers negotiate directly with manufacturers for rebates and use the PBM for other administrative services such as Drug Utilization Review ("DUR") and claims processing. Rebates are not passed down to plan beneficiaries; however, they may help reduce beneficiaries' overall insurance premium costs. Of note, rebates paid to PBMs have come under criticism as a key driver of drug costs[169] and have been the subject of recent reform efforts. Specifically, on November 20, 2020, the HHS Office of Inspector General ("OIG") promulgated a final rule amending the AKS safe harbor for discounts to eliminate protections for rebates or other price reductions from manufacturers to plan sponsors under Medicare Part D or PBMs acting on their behalf (commonly referred to as the "rebate rule").[170] Implementation of the rebate rule was first delayed to January 2023 pursuant to litigation filed by the Pharmaceutical Care Management Association ("PCMA") against HHS, and later delayed to 2026 by the Biden Administration.[171] Recent legislative proposals would prohibit the implementation of the rebate rule.[172] Separately, the Federal Trade Commission ("FTC") continues to monitor PBM practices and impacts of PBM industry consolidation. FTC established a working group to contemplate rulemaking, including competition rules with respect to rebates between manufacturers and third-party payers such as PBMs,[173] and has considered studying PBM reimbursement practices. On February 24, 2022, FTC issued a Request for Information ("RFI") seeking comment on the business practices of "large, vertically integrated" PBMs and "their impact on patients, physicians, employers, independent and chain pharmacies, and other businesses."[174] The RFI focuses on a wide range of issues in the PBM market, including contract terms, rebates, fees, pricing policies, among others.[175] States are also are engaged in ongoing efforts related to problematic PBM activities, including related to spread pricing, pricing and rebate transparency, and patient cost-sharing.
- **Creating pharmacy networks and negotiating lower dispensing fees.** PBMs create networks of pharmacies that agree to dispense prescription drugs under agreed-upon terms. PBMs negotiate a reimbursement rate for each drug product, as well as a dispensing

fee. When a plan beneficiary pays for a prescription, the pharmacy generally passes the copayment or coinsurance to a PBM, which then pays the pharmacy the negotiated reimbursement and dispensing fee. This arrangement allows the PBM to create spread-pricing profits and impose penalty fees on pharmacies that do not achieve contracted performance goals such as rate of generic dispensing. PBMs also may operate pharmacies themselves, including mail-order and specialty pharmacies. When payers and PBMs operate and drive utilization to their own pharmacies through narrow networks, they can negotiate additional bulk purchase discounts from manufacturers that are retained by the payer or PBM pharmacy.

Figure 10: The flow of funds in the pharmaceutical distribution system[176]



Various entities across the drug supply chain are increasingly contracting and consolidating, both horizontally and vertically. For example, three PBMs – Express Scripts, CVS Caremark, and OptumRx – control the majority of the market, together totaling an estimated 71% of Medicaid and Medicare Part D beneficiaries and 86% of the private market.[177] This demonstrates a high level of horizontal consolidation in the PBM industry. Further, these PBMs have some form of common ownership with large retail chains and/or specialty pharmacies, payers, and other entities, demonstrating an increasing level of vertical integration: CVS Caremark is affiliated with CVS and Aetna; Express Scripts is affiliated with Accredo and Cigna; and OptumRx is affiliated with BriovaRx and UnitedHealthcare. There is an emerging trend of large PBMs launching or aligning with GPOs (e.g., Zinc, Ascent, and Emisar), as well as health care provider services, health care management services, lab benefit managers, and other entities.

While PBMs generally consider vertical integration to be to the benefit of patients,[178] there are concerns that extensive consolidation has reduced transparency in the financial relationships among payers and other participants in the drug supply chain and may adversely impact patient

access due to significant bargaining power of the consolidated entities. On the other hand, PBMs generally have demonstrated success in keeping payers' net prices low and increasing the overall rate of price concessions achieved from manufacturers, providing a benefit to plans and payers. For example, a survey by the Pew Charitable Trust found that 91% of rebates were passed through to plans in 2016 (up from 78% in 2012).[179] PBMs retained roughly the same volume of rebates despite the higher rates of rebate pass-through due to an overall growth in rebate volume, including an estimated increase of manufacturer rebates from $39.7 billion in 2012 to $89.5 billion in 2016,[180] reflecting in part the impact of PBM bargaining power and negotiations.

Efforts to manage costs

Payers and PBMs have various tools at their disposal with which to control spending on prescription drugs. These tactics include:

- **Requiring greater cost sharing for high-cost products.** As indicated above, PBMs and payers have wide discretion to design formularies that determine how drugs are reimbursed, as well as the rate of patient cost sharing for drug products (although, for Medicare Part D plans, these formulary designs must adhere to federal requirements and be approved by CMS). Tiered formularies are used to steer patients toward generics and branded drugs for which there exists no generic equivalent by requiring lower cost sharing for these drugs. Within a given formulary, tier 1 generally includes covered generic drugs (also called "preferred drugs"), and tier 2 generally includes preferred branded drugs for which there is no generic equivalent. Traditionally, PBMs used a three-tier structure, placing non-preferred drugs in tier 3. Today, many PBMs utilize a four-tier or five-tier structure, reserving the highest tiers (tiers 3, 4, or 5) for high-cost specialty drugs. PBMs shift a significant portion of the cost for non-preferred drugs to the patient, in the form of higher copayments (fixed dollar amounts) or coinsurance (a percentage of the cost of the drug). Negotiations with manufacturers typically involve the use of bidding tables where each manufacturer offers varying levels of rebates for exclusive, preferred, or parity formulary placement within competitive therapeutic classes (i.e., diabetes) where multiple clinically effective treatments are available for prescribing. Manufacturer bidding for government payer lives is typically separated from bidding activity for commercial payer lives due to the different coverage and reimbursement dynamics of each market. A developing trend is to show physicians the relative formulary status of a treatment option within their electronic health records at the time of prescribing, in order to better align the physician's decisions with the lowest cost option for the patient, employer, or health system.[181]
- **Utilization controls.** PBMs and insurance plans frequently require patients to obtain prior authorization before covering expensive medications. PBMs and insurance plans may also require a patient to try a preferred product (usually a lower cost generic) before agreeing to reimburse a more expensive product, a process known as "step therapy" or "fail first". Additionally, plans and PBMs may block coverage of certain drugs altogether, or utilize narrow pharmacy networks to limit patient access.
- **Mandatory substitution of generics.** Most state Medicaid plans require pharmacies to dispense a generic version of a drug product, if available, unless the patient's prescriber specifies that the branded version is medically necessary. Payers and PBMs also may encourage or require generic substitution, state law permitting. Multiple states require pharmacists to replace brand-name drugs with generics, unless a prescriber affirmatively blocks pharmacist substitution.[182]
- **Cost-sharing/copayment accumulators and maximizers.** PBMs and insurance plans

have increasingly utilized benefit designs, such as accumulators and maximizers, to minimize and/or capture the effect of drug manufacturer copayment assistance. Under accumulator programs, the plan does not allow the value of manufacturer copayment assistance to count toward the beneficiary's deductible or out-of-pocket maximum. Thus, once the copayment assistance is exhausted, the beneficiary must pay the entire amount of his or her deductible before plan benefits are available. Under a maximizer program, the plan aligns the beneficiary's copayment obligation with available copayment assistance from manufacturers (i.e., by dividing the annual maximum benefit to set monthly copayment amounts for beneficiaries). Manufacturer assistance applies to the beneficiary's copayment obligation but not toward the beneficiary's deductible or out-of-pocket maximum. Accumulator and maximizer programs are subject to ongoing policy activity.

- Recent federal rulemaking clarifies that accumulator programs (and, by extension, any accumulator elements included in maximizer programs) are expressly permitted for health plans sold on the Affordable Health Insurance Exchanges, as well as most other plans, to the extent permitted by state law.[183] Additionally, in December 2020, CMS revised the methodology for calculating AMP and best price as part of the Medicaid Value-Based Purchasing Final Rule to require, beginning in 2023, that manufacturers "ensure" that the full value of the copayment assistance is passed on to the patient and is not subject to accumulator programs in order to exclude such assistance from AMP and best price calculations.[184] The Pharmaceutical Research and Manufacturers of America ("PhRMA") challenged these provisions,[185] which were vacated by the D.C. District Court in May 2022.[186]
- Certain states have proposed and/or enacted legislation to address copayment accumulators and maximizers. As of 2022, 14 states and Puerto Rico have enacted provisions that restrict or effectively prohibit accumulator programs by requiring health care plans to apply any third-party payments, such as copayment assistance from manufacturers, toward a patient's cost-sharing obligations.[187] Between 2021 and 2022, eight states enacted some form of cost-sharing or coupon legislation.[188] For example, Kentucky legislation prevents insurers and PBMs from excluding any copayment assistance provided to beneficiaries when calculating cost-sharing requirements.[189] This is a rapidly evolving area with significant variation at both the state and federal policy levels.

- **Benefit carve-out or "lasering" programs.** A number of vendors offer benefit carve-out or "lasering" programs, which encourage plan sponsors or issuers to "laser" certain specialty drugs out of their drug formularies on the theory that claims for those drugs will be paid by manufacturer financial assistance programs (or, potentially, non-manufacturer, needs-based charity funding). These lasering programs adjust plan benefits to shift the cost of prescription drugs from the plan to manufacturers (for example, where assistance may be provided to patients who are "functionally uninsured" due to lack of coverage for a product) or other sources of assistance. Lasering programs generally operate by listing specialty drugs with manufacturer assistance programs in the highest tier, and when a patient attempts to fill a specialty drug within that tier, the claim is denied. The vendor then contacts the patient and enrolls the patient into a manufacturer assistance program, and the claim is submitted with the new assistance information. The vendor typically retains a portion of the plan savings and/or charges the plan a fee for access to their services.
- **Value-based contracts.** Manufacturers and payers are increasingly negotiating agreements to link the purchase price to clinical outcomes or financial measures, especially in chronic conditions and where medical cost offsets can be significant for the use of a

drug. These arrangements are sometimes referred to as value-based contracts ("VBCs"), outcomes-based contracts ("OBCs"), or performance-based risk sharing agreements ("PBRSAs").[190] A number of legal and regulatory requirements may be implicated by these arrangements. For example, the federal AKS prohibits anyone from soliciting, receiving, offering, or paying any remuneration in return for a referral for an item or service that may be paid for by a federal health care program.[191] Statutory and regulatory safe harbors protect certain arrangements from AKS liability, including qualifying discount and warranty arrangements,[192] but there is some uncertainty with respect to how these safe harbors apply to VBC arrangements. Recently enacted value-based enterprise safe harbors may protect certain arrangements with a value-based purpose; however, these safe harbor protections do not generally apply to manufacturers and other drug supply chain entities, with a narrow exception for in-kind digital tools provided by certain entities in care coordination. VBCs also may raise risks related to price reporting obligations, as the terms of such agreements can lead to significant variance in pricing at the per-patient level and potentially drop unit prices for certain patients below the "best price" otherwise offered for the drug product. Manufacturers may report value-based purchasing ("VBP") arrangements under one of two methodologies: (1) under a bundled sales approach, which has been traditionally employed by manufacturers to distribute any VBP discount proportionally to the total dollar value of all units sold as part of the bundled arrangement; or (2) under a "multiple best prices" approach, to report multiple best price points for a single dosage form and strength to reflect the discounts or prices available under the VBP.[193] VBCs also may raise issues related to off-label promotion, for instance, if there is a need to share data on potential outcomes that are helpful to identify value but are not otherwise included in product labeling. FDA guidance expressly permitting the communication of health care economic information ("HCEI") related to approved labeling lowers the risk related to such communications, and FDA has stated explicitly that it does not regulate terms for VBCs.[194]

- **Cost-effectiveness assessments.** PBMs and payers make coverage determinations based on certain cost-effectiveness information, including, where available, assessments similar to HTAs in other countries, such as the National Institute for Health and Care Excellence ("NICE") in the United Kingdom. For example, Innovation and Value Initiative ("IVI") is a nonprofit research organization that seeks to "advance the science, practice, and use of value assessment in healthcare to make it more meaningful to those who receive, provide, and pay for care."[195] One of IVI's projects, the Open-Source Value Project, aims to develop disease-specific value assessment models, which are created with the input of multiple stakeholders and public comment.[196] The Institute for Clinical and Economic Review ("ICER") is a nongovernmental entity that produces reports analyzing evidence on the effectiveness and value of drugs and other medical services in the U.S.[197] ICER assesses the value of a medical intervention with four elements: (1) comparative clinical effectiveness; (2) incremental cost-effectiveness; (3) other benefits or disadvantages; and (4) contextual considerations.[198] The assessments utilize the Quality-Adjusted-Life-Year ("QALY") to compare incremental cost-effectiveness of care options, but also presents cost per life year gained and cost per equal value life year gained.[199]

Efforts to facilitate access

A. Manufacturer financial assistance

Manufacturers frequently provide financial assistance or free products to patients in order to facilitate access. Such assistance may include manufacturer-sponsored patient assistance

programs ("PAPs") (i.e., free drugs or diagnostic services), commercial copayment assistance (i.e., copayment coupons), and assistance provided by independent, third-party charitable entities (often referred to as "independent charity PAPs"). Eligibility for these types of programs may depend on income level, insurance status, and type of insurance. Additionally, manufacturers often provide other support services, such as assistance with navigating insurance coverage for specialty drugs.

Financial assistance to patients is highly regulated, particularly where this assistance is provided by drug manufacturers. The AKS limits the ability of manufacturers to provide coupons or discounts to patients enrolled in government health care programs, prohibiting manufacturers from providing direct subsidies to offset their out-of-pocket expenses for copayments and deductibles.[200] Although free drug programs for financially needy patients have historically not raised extensive concerns under anti-kickback laws, the HHS OIG, which is tasked with identifying and combating waste, fraud, and abuse within HHS, has articulated concerns with PAPs related to Medicare Part D.[201] For example, PAPs and copayment coupons may increase costs to the federal government under Medicare Part D because cost-sharing subsidies for Part D-covered drugs that count toward patients' true out-of-pocket expenses ("TrOOP") will increase the number of beneficiaries who qualify for catastrophic benefit in any given coverage year and the point during the year at which they reach the catastrophic benefit.[202] PAPs may also have the effect of locking beneficiaries into the manufacturer's products, even if there are other equally effective, less costly alternatives, and patients may transition from a PAP to a government program such as Medicare Part D at some point in time.[203] OIG reiterated its position against manufacturer assistance related to Medicare Part D as recently as 2020, finding that a proposal to provide copay assistance to Part D beneficiaries would be "highly suspect" under the AKS.[204] The OIG has also scrutinized charitable organizations that are not truly independent from manufacturer donors.[205] For example, OIG is concerned about independent charity PAPs defining disease-specific funds so narrowly that a donor earmarking funds for a given disease fund effectively results in subsidization of the donor's own products.[206] OIG has recently issued a number of favorable advisory opinions regarding assistance programs, ranging from covering administration of one-time treatment to providing other services, such as transportation and housing during treatment or sponsored testing.[207]

B. Coverage of off-label use

In general, drug products must have FDA approval to be reimbursed by public or private payers. Coverage for "off-label" use of approved products – drugs used for a different disease or medical condition, given in a different way, or given in a different dose than specified in the approved label[208] – may be available in certain circumstances. For example, Medicare Part D covers drugs prescribed for off-label use if the drugs are listed in CMS-recognized compendia for determining medically accepted indications.[209] Under Part B, reimbursement for off-label use is permitted if the MAC determines the use to be medically accepted, taking into account the major drug compendia, authoritative medical literature, and/or accepted standards of medical practice.[210] State Medicaid programs mandate coverage of off-label uses where the drug is listed in CMS-recognized compendia.[211] Additionally, many states also currently require Medicaid programs and private payers to cover off-label use of drugs that meet certain criteria, with some requiring off-label coverage only for certain disease states such as cancer or other life-threatening or chronic and seriously debilitating conditions, and others mandating off-label coverage more broadly.[212] Off-label use is particularly widespread in oncology, where payers often use independent National Comprehensive Cancer Network Drugs and Biologics Compendium ("NCCN") guidelines to cover off-label treatments.

Off-label use remains controversial. On the one hand, off-label use may represent a physician's determination regarding which treatment would be medically appropriate for a given patient and is an important aspect of the physician-patient relationship. On the other hand, many off-label uses are being prescribed without strong evidence of their safety or efficacy in treating the off-label indication, raising patient safety concerns.[213] In any case, communications regarding off-label use outside of the physician-patient relationship are highly regulated, and manufacturers are prohibited from promoting drug products for any off-label use (although certain communications with payers or other communications consistent with labeling may be permissible).[214]

C. Expanded access and right to try

Even if reimbursement for unapproved drugs is not available, patients may gain access to investigational drug products through FDA's expanded access or "compassionate use" program. Expanded access allows patients with an immediately life-threatening condition or serious disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.

There are three types of expanded access investigational new drugs ("INDs"): individual patient expanded access INDs, including for emergency use;[215] intermediate-size patient population expanded access INDs;[216] and treatment INDs for widespread use.[217] In all cases of expanded access use, FDA must determine that: (1) the patient(s) to be treated "have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy"; (2) the potential patient benefit justifies the potential risks, and the risks are reasonable given the disease or condition to be treated; and (3) granting the expanded access "will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use".[218] Additional criteria apply to each type of expanded access.

As a separate pathway, federal and state "right to try" laws permit patients with life-threatening diseases to access certain unapproved therapies without going through the FDA expanded access process. Following recent enactment of state-level laws in a significant majority of states,[219] the federal Right to Try Act was signed into law in 2018 to permit access to investigational drugs.[220] Under the federal Act, eligible patients must be diagnosed with a life-threatening disease or condition, have exhausted approved treatment options and be unable to participate in a clinical trial involving the eligible investigational drug, and have provided written informed consent.[221] Manufacturers have discretion over whether to make their products available to patients who qualify for access under the law.

D. Digital health solutions

Manufacturers are also increasingly looking toward digital health tools to facilitate access to prescription drugs and improve communications and outcomes across the care continuum. Digital health solutions encompass a wide range of items and services, ranging from telehealth services to phone applications ("apps") to wearables (i.e., Fitbit) to prescription digital therapeutics. Manufacturers may utilize digital health for real-time data generation as well as personalizing products and services for patients. Where appropriate, certain digital health tools may qualify in and of themselves for coverage and reimbursement.

CMS has gradually expanded the codes available for certain products (i.e., prescription digital behavioral therapies) as well as services associated with digital health offerings. For example, CMS has added remote patient monitoring ("RPM") codes, which require

the collection of physiologic data that is digitally uploaded and is limited to use with established patients, as well as remote therapeutic monitoring ("RTM") codes, which focus on non-physiological treatment management services and cover services such as remotely monitoring a patient's therapy adherence via patient-reported data.[222] These and other updates might enable wider innovation and commercialization of digital health solutions.

Policy issues that affect pricing and reimbursement

Cost of innovation, U.S. drug pricing, and "Foreign Underpricing"

Amidst global controversy over the high prices of innovative drug products, there is ongoing debate regarding whether drug prices reflect the cost of innovation and, if so, whether this cost is appropriately distributed. The anticipated cost of developing a new drug, inclusive of capital costs and money spent on candidate drugs that fail to reach the market, has been estimated to range from less than $1 billion to more than $2 billion, and only about 12% of drugs succeed in the clinical trial process.[223] According to one study, the cost to develop a new prescription drug that gains marketing approval is estimated to be $2.6 billion as of 2013.[224] This is a significant increase from $802 million in 2003 (approximately $1 billion in 2013 dollars), representing a 145% increase in the 10-year time period between studies. Accounting for post-approval R&D, the cost of total development increases to nearly $2.9 billion.[225] Key drivers of this significant cost include high failure rates for potential clinical drug candidates (an estimated seven out of eight compounds that enter the clinical testing pipeline fail in development) as well as high out-of-pocket clinical costs for drug trials, including increased complexity or clinical trial design and larger trials, higher cost of inputs, increased focus on targeting chronic and degenerative diseases, changes in protocol design to include efforts to gather HTA information, and testing on comparator drugs to accommodate payer demands for comparative effectiveness data.[226]

The cost of innovation appears to fall disproportionately on the U.S., where drug prices far outpace prices in other countries. In 2020, the CEA issued a report evaluating how the costs and benefits of medical innovation are distributed across developed nations. According to the CEA, while "[t]he U.S. Government and the biopharmaceutical industry have been critical to improving health worldwide by leading the way in the [R&D]", "foreign countries often do not make equal investments in the R&D that is necessary to fuel innovation and ensure the economic viability of biopharmaceutical products".[227] The report found that foreign "free-riding" has increased over the past 15 years, with patented drug prices in European countries falling from 51% of U.S. prices in 2003 to about 32% of U.S. prices in 2017.[228] The CEA concluded that "[f]oreign governments have implemented stricter price controls, enabling these products to be sold below fair market value, with Americans picking up the tab for making the availability of such products feasible in the first place", leading to a "slower pace of innovation" and "fewer potential new life-saving therapies for patients in all countries".[229] By contrast, "[r]educing foreign price controls would increase profits and innovation, thereby leading to greater competition and lower prices for U.S. patients".[230]

Addressing U.S. drug prices has been the subject of significant debate. Reform proposals range from addressing payment and reimbursement of drug prices in the U.S., to exercising trade policy tools to combat drug pricing practices in foreign markets.[231] Additionally, states are actively considering proposals that would address drug pricing practices by a variety of mechanisms. These issues are explored in more detail in the following section on emerging trends.

Emerging trends

A number of federal- and state-level policy proposals could affect the pricing and reimbursement of drugs in the U.S. This section discusses these emerging proposals.

Federal Government Negotiation of Medicare Drug Prices

Under current law, the HHS Secretary is not permitted to negotiate Medicare drug prices. Legislative proposals would allow the federal government to negotiate prices directly with drug manufacturers for certain Part B and Part D single source drugs.[232] The negotiation process would involve establishing an upper limit for the negotiated price (the "maximum fair price") based on an "applicable percent" of the average non-federal AMP: 75% of non-federal AMP for drugs more than nine years but less than 12 years beyond approval; 65% of non-federal AMP for drugs 12–16 years after approval; and 40% of AMP for drugs 16 or more years after approval.[233] Medicare's payments for Part B drugs negotiated under this proposal would be 106% of the maximum fair price, as opposed to 106% of ASP under current law.[234] In addition, an excise tax would be imposed on manufacturers that do not comply with the negotiation process.[235]

Inflation penalties

In addition, proposed legislation would establish mandatory rebates for certain Part B and Part D drugs with prices that have increased faster than the rate of inflation.[236] The rebate amount would be calculated as the total number of units, including both Medicare and the commercial market, multiplied by the amount by which the price exceeded the inflation benchmark during a certain year.[237] Price changes would be based on ASP for Part B drugs and AMP for Part D drugs.

Part D redesign

Legislative proposals have included provisions to "redesign" the Medicare Part D benefit, including changes such as a $2,000 cap on beneficiary out-of-pocket spending (with increases each year based on increases in *per capita* Part D costs), elimination of the "coverage gap" phase by extending the initial coverage phase up to the catastrophic phase, and elimination of beneficiary cost sharing in the catastrophic phase.[238] Part D redesign also would reallocate liabilities between beneficiaries, manufacturers, plans, and Medicare.[239]

PBM oversight

Recent drug pricing reform proposals include provisions that would require PBMs to submit regular reports to plan sponsors related to drug costs, utilization, and spending.[240] These reports would be submitted every six months and include details such as the total amount of copayment assistance dollars paid, or copayment cards applied, that were funded by the drug manufacturer, a list of each covered drug that was dispensed during the report period, a list of each therapeutic category or class of drugs that was dispensed, the total gross spending on prescription drugs, the total net spending on prescription drugs, among other items.[241] PBMs also would be required to identify rebates, fees, and other remuneration received from entities such as manufacturers and paid to entities such as brokers and consultants.[242] The first four reports submitted to the plan sponsor also would be submitted to the Comptroller General, and failure to submit timely or accurate reports could lead to Civil Monetary Penalties ("CMPs").

Reference pricing

Given disparities between U.S. and ex-U.S. drug prices, a number of proposals have considered tying drug prices for certain U.S. payers to prices in international markets, a practice referred to as "reference pricing". For example, the Trump Administration issued an interim final rule, commonly referred to as the Most Favored Nation Final Rule ("MFN

Rule"), which would have tied Medicare Part B payments for certain drugs to the lowest price paid in other economically advanced countries;[243] however, this rule ultimately was enjoined and rescinded.[244] Legislative proposals related to drug price negotiation also have included reference pricing provisions,[245] but these proposals were not enacted. Certain states have proposed and enacted reference pricing proposals. For example, California's June 2020 public health omnibus (AB-80) amended the state's definition of "best price" to mean "the manufacturer's lowest price available to any foreign or domestic class of trade organization or entity",[246] effectively expanding Department of Health Care Services ("DHCS") authority to negotiate state supplemental rebates based on best prices offered by manufacturers internationally, rather than just purchases within the U.S. In addition, in August 2020, the National Academy for State Health Policy ("NASHP") put forth model legislation to authorize a state's department of insurance to establish international reference rates (based on drug prices in four Canadian provinces) as the upper payment limit for the 250 most costly drugs in that state for participating purchasers.[247]

Drug importation

The U.S. recently adopted a slight expansion in wholesalers' and pharmacists' ability to import drugs. Drug importation is highly regulated, and the only foreign-manufactured drug that can be legally imported into the U.S. for commercial use without authorization by the drug's manufacturer is a drug that appears on FDA's drug shortage list or a drug that is imported pursuant to section 804 of the FDCA.[248] Section 804 of the FDCA authorizes pharmacists and wholesalers to import prescription drugs from Canada, provided certain conditions are met.[249] In order for section 804 to take effect, the HHS Secretary must certify to Congress that it "poses no additional risk to the public's health and safety" and "results in a significant reduction in the cost of covered products to the American consumer".[250] The Secretary made that certification to Congress in September 2020, and in October 2020, the federal government finalized regulations to implement section 804. Those regulations permit states and Indian Tribes to submit proposals to FDA regarding the importation of prescription drugs from Canada upon demonstrating that the importation program will pose no additional risk to the public's health and safety and "will result in a significant reduction in the cost of covered products to the American consumer".[251] PhRMA challenged the rule based on safety and other concerns,[252] and litigation is ongoing. The U.S. also has considered legislative proposals related to the personal importation of drug products.

Accelerated approval process

The U.S. has considered legislation that would affect accelerated approval, a process that allows FDA to approve drugs that "treat serious conditions, and that fill an unmet medical need" based on a surrogate or intermediate clinical endpoint; when a drug is approved through the accelerated approval process, the manufacturer is required to conduct post-marketing clinical trials to verify and describe the drug's benefit. Since accelerated approval became available in 1992, 278 drug and biologics have been approved through the process for a broad range of serious conditions, including HIV/AIDS, various forms of cancer, and other conditions.[253] There have been proposals to amend the accelerated approval process, including with respect to changing withdrawal criteria or providing for automatic expiration. Certain payers also have considered proposals to limit coverage for certain accelerated approval products.[254]

Additional state-level proposals related to drug pricing reform in the U.S.

States continue to be active with respect to drug pricing reform proposals. A significant number of states have proposed and enacted transparency laws that require manufacturers,

PBMs, insurers, and other entities to report certain drug pricing information to state agencies.[255] While reporting requirements vary by state, these laws generally require manufacturers to report information regarding drug prices and drug price increases above a certain threshold.[256] States have adopted other mechanisms for price reporting, such as authorizing an independent board to compile a list of drugs on which the state spends significant dollars and/or for which the WAC has increased significantly over a period of time.[257] States also are considering and adopting proposals related to generic manufacturing, drug importation, prescription drug affordability review boards, anti-price gouging and price increase penalties. Although state laws related to drug pricing are proliferating, a number of these laws have been subject to legal challenges or struck down by the courts.[258]

Successful market access

As demonstrated by this chapter, the drug pricing and reimbursement infrastructure in the U.S. consists of a complex patchwork of policies and institutions. Successful market access requires navigating this infrastructure in a way that ensures drug products are available to patients, reimbursable by patients' health care plans, and appropriately valued. These efforts must be compliant with various overlapping regulatory requirements and minimize enforcement risk under the AKS, FCA and other federal and state laws.[259]

Accordingly, drug manufacturers and investors funding development of drug products should consider the following in designing both U.S. and global market access strategies:

- **Access.** Manufacturers should evaluate the criteria for favorable coverage under various private and public plans and coordinate appropriate engagement with PBMs facilitating coverage with these payers, as well as the relative use by patients who are covered under government *versus* private payers and the likely settings of care for one-time or chronic use of the product. Successful market access strategies will include plans for patient assistance and patient support services, pharmacy and wholesaler distribution networks, and other key features facilitating access to drug products.
- **Pricing.** Manufacturers should investigate the coverage, coding, and payment structures that will apply to their drug products for each payer type in the U.S. Pricing strategies should include conducting a reimbursement assessment, including comprehensive coding and payment analysis across all relevant settings of care, and developing rebate bidding and contracting strategies, preparing payer budget impact moles, conducting payer market research, and using HCEI to support the proposed pricing structure. Manufacturer list and net pricing scenarios for new products must account for all supply chain concessions over a multi-year time horizon with growing limitations on ability to increase pricing year over year, as well as model impacts based on government price reporting obligations (e.g., best price, AMP, and ASP) and mandatory rebate liabilities (e.g., MDRP).
- **Value.** Manufacturers should develop appropriate evidence, including real world evidence, and messaging to communicate the value proposition for their drug products, including by developing a thorough understanding of the prescribing pathway, comparator treatments, quality measures, patient need, and direct and indirect costs of treatment with the new drug. Manufacturers should prepare to demonstrate the cost-effectiveness of drug products, in the event of a potential ICER assessment or requests for such information from payers more generally. Consideration should be given to potential value-based pricing structures that link the purchase price to patient outcomes and product warranties, as well as provide more predictable cost outlays for both government and private payers.

If possible, manufacturers should develop U.S. market access strategies at least two years before approval and launch in the U.S. and integrate these strategies with global market access efforts. When appropriately structured, market access strategies can inform clinical development and clinical trial outputs, help guide positioning during the drug approval process, and facilitate market entry upon approval. Market access strategies also should include frequent review and updates based on changes in the U.S. reimbursement framework. The payers and programs involved in drug coverage and reimbursement are constantly evolving, and current or future proposals for reform and growing government enforcement activity focused on market access could significantly impact drug pricing in the U.S.

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30. *See* Julie A. Patterson & Norman V. Carroll, *Should the United States Government Regulate Prescription Process? A Critical Review*, 16 Research in Social and Administrative Pharmacy 717 (2020); *see also* Ashish Kumar Kakkar, *Pharmaceutical Price Regulation and Its Impact on Drug Innovation: Mitigating the Trade-Offs*, 31 Expert Opinion on Therapeutic Patents 189 (2021), *available at* https://www.tandfonline.com/doi/full/10.1080/13543776.2021.1876029 ("[B]etween 1985 and 2004 there was a significant reduction in the R&D spending by EU pharmaceutical firms resulting in introduction of 46 fewer drugs.") (internal citations omitted); *see also* Neeraj Sood *et al.*, *The Effect Of Regulation On Pharmaceutical Revenues: Experience In Nineteen Countries*, HealthAffairs (Dec. 16 2008), https://www.healthaffairs.org/doi/10.1377/hlthaff.28.1.w125 ("[I]t is important to note that revenue reductions will affect future innovation. For example, price regulation can delay the launch of new drugs, and limit the availability of new drugs.") (internal citations omitted). *See also* U.S. Trade Rep., *2020 Special 301 Report* 15-16 (Apr. 2020), https://ustr.gov/sites/default/files/2020_Special_301_Report.pdf (raising concerns that "[p]ricing and reimbursement systems in foreign markets that are not market-based, or that do not otherwise appropriately recognize the value of innovative medicines and medical devices . . . undermine incentives for innovation in the health care sector.")
31. Heather M. O'Neill & Lena Clarissa Crain, *The Effects of Price Regulation on Pharmaceutical R&D and Innovation*, 5 Bus. & Econ. Faculty Publications 61 (2005) ("In Germany, increased price regulations were implemented in 1992 through the Health Sector Act. By restricting prices, profits were diminished and companies saw much less incentive to conduct R&D in Germany. From 1992–1999, 23,000 jobs were eliminated in the German pharmaceutical industry, and by 2001, Germany had slipped from the number one to the number three position in European countries conducting innovative R&D.")
32. Council of Econ. Advisers, *Funding the Global Benefits to Biopharmaceutical Innovation* 11 (Feb. 2020), https://trumpwhitehouse.archives.gov/wp-content/uploads/2020/02/Funding-the-Global-Benefits-to-Biopharmaceutical-Innovation.pdf.
33. 21 U.S.C. § 393(b)(1)–(2). FDA initially was established as the Bureau of Chemistry within the Department of Agriculture with the 1906 Pure Food and Drugs Act. Pub. L. No. 59-384, 34 Stat. 768, (1906). The 1906 Act banned interstate traffic in adulterated

and mislabeled products, provided criminal penalties for violations, and authorized the seizure of offending products, but did not authorize the FDA to require premarket testing or approval for new drug products. The agency assumed its current gatekeeper role through the 1938 Federal Food, Drug, and Cosmetics Act ("FDCA"). Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended in scattered sections of 21 U.S.C.). The original FDCA required manufacturers to notify the agency and submit evidence of safety before marketing new drugs to the public. The subsequent 1962 Amendments transformed this premarket *notification* system in a premarket *approval* system, under which the agency must affirmatively approve new drugs on the basis of safety *and* efficacy. Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962); *see also, e.g.*, Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 Va. L. Rev. 1753, 1764–65 (1996).

34. *Fact Sheet: FDA at a Glance*, U.S. Food & Drug Admin. (Nov. 2020), https://www.fda.gov/media/143704/download.
35. 21 U.S.C. § 355 (NDAs); 42 U.S.C. § 262 (BLAs).
36. 21 U.S.C. § 355(d) (NDAs); 42 U.S.C. § 262(a)(2)(C) (BLAs).
37. 21 U.S.C. § 355(j) (ANDAs); 42 U.S.C. § 262(k) (biosimilar applications).
38. 21 U.S.C. § 355(j)(8)(B) (ANDAs); 42 U.S.C. § 262(i)(2)(B) (biosimilar applications).
39. *Novel Drug Approvals for 2021*, U.S. Food & Drug Admin., https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2021 (content current as of Jan. 6, 2022) (noting approval of 50 drug and biological products by the Center for Drug Evaluation and Research, and excluding from this list vaccines, allergenic products, blood and blood products, plasma derivatives, cellular and gene therapy products, or other products approved by the Center for Biologics Evaluation and Research); *2021 Biological License Application Approvals*, U.S. Food & Drug Admin., https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/2021-biological-license-application-approvals (content current as of Dec. 21, 2021) (noting approval of 13 biological products); *2021 First Generic Drug Approval*s, U.S. Food & Drug Admin., https://www.fda.gov/drugs/drug-and-biologic-approval-and-ind-activity-reports/2021-first-generic-drug-approvals (content current as of Feb. 10, 2022) (defining "first generics" as the first approval by FDA which permits a manufacturer to market a generic product in the U.S.); *Biosimilar Product Information*, U.S. Food & Drug Admin., https://www.fda.gov/drugs/biosimilars/biosimilar-product-information (content current as of Feb. 25, 2022).
40. Pub. L. No. 102–571, 106 Stat. 4491 (1992).
41. *Fact Sheet: FDA at a Glance*, U.S. Food & Drug Admin., https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance (content current as of Nov. 18, 2021).
42. U.S. Food & Drug Admin., PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 Through 2022 6, https://www.fda.gov/media/99140/download (last visited May 13, 2020).
43. *Id.*
44. Priority review is also available to manufacturers that have a priority review voucher or where other criteria are met. *See, e.g.*, *Guidance for Industry, Expedited Programs for Serious Conditions—Drugs and Biologics*, U.S. Food & Drug Admin., 24–25 (May 2014), https://www.fda.gov/media/86377/download.
45. 21 U.S.C. §§ 356(a) (breakthrough therapy designation), 356(b) (fast track designation), 356(c) (accelerated approval); *see also* 21 C.F.R. part 314, subpart H; 21 C.F.R. part 601, subpart E; U.S. Food & Drug Admin. *Guidance for Industry,*

Expedited Programs for Serious Conditions—Drugs and Biologics (May 2014), https://www.fda.gov/media/86377/download. Additional pathways and designations may also be available. *See, e.g.*, 21 U.S.C. §§ 356(g) (Regenerative Advanced Therapy designation), 356(h) (Limited Population Pathway for Antibacterial and Antifungal Drugs), 355f(d) (Qualified Infectious Disease Product designation).

46. 21 U.S.C. §§ 355(c)(3)(E)(ii), 355(j)(5)(F)(ii); 21 C.F.R. § 314.108.
47. 21 C.F.R. § 314.108(b)(2). An NDA or ANDA can be submitted after four years if it contains a certification of patent invalidity or noninfringement.
48. 21 U.S.C. §§ 355(c)(3)(E)(iii), 355a(b), 360cc(a); 42 U.S.C. § 262(k)(7); 21 C.F.R. §§ 314.108, 316.31.
49. 21 U.S.C. §§ 360n, 360ff, 360bbb-4a.
50. In many cases, the definitions provided herein are summaries of statutory or regulatory definitions.
51. 42 C.F.R. § 447.502.
52. 42 U.S.C. § 1396r-8(k)(1).
53. *Id.* § 1395w-3a(c)(1).
54. *Pricing Policy Update: Important Information About AWP Data*, Wolters Kluwer, https://www.wolterskluwer.com/en/solutions/medi-span/about/pricing-policy-update (last visited June 2, 2021).
55. 42 U.S.C. § 1396r-8(c)(1)(C).
56. *Id.* § 1395w-3a(c)(6)(B).
57. Social Security Amendments of 1965, Pub. L. No. 89-97, tit. XVIII, 79 Stat. 286, 291–343 (1965).
58. 42 U.S.C. § 1395y(a)(1)(A).
59. *Id.* § 1395c *et seq*.
60. *Id.* § 1395kk-1.
61. *Id.* §§ 1395ff(f)(1)(B), 1395ff(f)(2)(B); *see also* Ctrs. for Medicare & Medicare Servs., *Medicare Program Integrity Manual*, ch. 13, § 13.1.1, https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/ Downloads/pim83c13.pdf (last updated Feb. 12, 2019).
62. 42 U.S.C. § 1395j *et seq*.
63. *Id.* § 1395k(a).
64. Some low-income beneficiaries may qualify for premium and cost-sharing assistance, either by qualifying for full Medicaid benefits or Medicare Savings Programs. *Id.* § 1396u-3.
65. *Id.* § 1395kk-1.
66. *Id.* §§ 1395j-1395w-6.
67. *Id.* § 1395w-21. MA plans are either local plans that serve a particular area, or regional plans that contract with CMS to provide services to one or more defined regions. Beneficiaries may choose to enroll in MA if there is a plan offered in their area. *Id.* § 1395w-28(4)–(5).
68. *Id.* § 1395w-22(a).
69. *Id.* § 1395w-22(a)(3); 42 C.F.R. § 422.100(c).
70. 42 U.S.C. § 1395w-131.
71. *Id.* § 1395w-101.
72. *Id.* § 1395w-104(b)(3)(C); *see also id.* § 1395w-104(b)(3)(G) (setting forth specified categories for which plans must include all covered Part D drugs). CMS automatically approves formulary classification systems that are consistent with the U.S. Pharmacopeia ("USP") category and class system. Alternative classification systems

must be reviewed by CMS to determine if they are sufficiently similar to the USP or other common systems, such as the American Hospital Formulary Service classification system. *See* Ctrs. for Medicare & Medicaid Servs., *Medicare Prescription Drug Benefit Manual*, ch. 6 § 30.2.1, https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Part-D-Benefits-Manual-Chapter-6.pdf (last updated Jan. 1, 2016).

73. 42 C.F.R. § 423.272(b)(2); *see generally* Cong. Research Serv., R40611, Medicare Part D Prescription Drug Benefit (2018).
74. 42 U.S.C. § 1395y(a)(1)(A); 42 C.F.R. § 411.15(k).
75. 42 U.S.C. § 1395w-102(e); 42 C.F.R § 423.100.
76. 42 U.S.C. § 1395ff; Ctrs. for Medicare and Medicaid Servs., *Decision Memo for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease*, Medicare Coverage Database (Aug. 7, 2022), https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=305; Ctrs. for Medicare and Medicaid Servs., *Decision Memo for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers (CAG-00451N)*, Medicare Coverage Database (Aug. 7, 2019), https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=291.
77. Ctrs. for Medicare & Medicaid Servs., *Medicare Program Integrity Manual*, ch. 13, § 13.2.2.3, https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/pim83c13.pdf (last updated Feb. 12, 2019).
78. Ctrs. for Medicare & Medicaid Servs., *Medicare Prescription Drug Manual*, ch. 6, § 30, https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Part-D-Benefits-Manual-Chapter-6.pdf (last updated Jan. 15, 2016); *see also* Ctrs. for Medicare & Medicaid Servs., *Medicare Managed Care Manual*, ch. 4, § 10.1, https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/mc86c04.pdf (last updated Apr. 22, 2016) (referring to the "Medicare Prescription Drug Manual" for requirements prescription drug coverage).
79. 42 U.S.C. § 1395w-104(b)(3)(A); 42 C.F.R. § 423.120(b)(1); *see also* Ctrs. for Medicare & Medicaid Servs., *Medicare Prescription Drug Benefit Manual*, ch. 6, § 30.1.5, https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Part-D-Benefits-Manual-Chapter-6.pdf (last updated Jan. 15, 2016).
80. 42 C.F.R. § 423.120(b)(2)(i).
81. 42 U.S.C. § 1395w-104(b)(3)(G)(iv). These classes of drugs are often referred to as "protected classes".
82. Social Security Amendments of 1983, Pub. L. No. 98-21, 97 Stat. 65 (1983).
83. 42 U.S.C. § 1395cc(a)(1)(H).
84. 42 C.F.R. § 412.2.
85. *Id.* § 412.60.
86. *Id.* § 412.2(f).
87. *Id.* §§ 412.150-412.172.
88. *Id.* § 412.22.
89. Medicare Payment Advisory Comm'n, *Hospital Acute Inpatient Services Payment System* 2 (Nov. 2021), https://www.medpac.gov/wp-content/uploads/2021/11/medpac_payment_basics_21_hospital_final_sec.pdf.
90. *See* 42 U.S.C. §§ 1395k(a)(1) (providing for coverage of medical or other health services), 1395x(s)(2) (defining medical and other health services to include drugs not usually self-administered).
91. 42. C.F.R. § 419.2(a).

92. Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003).
93. 42 U.S.C. § 1395w-3a(b). For certain drug products that lack ASP data, reimbursement payments may be calculated using the WAC. *Id.* § 1395w-3a(c)(4). WAC may also be used if lower than the ASP. *Id.* § 1395w-3a(b)(4).
94. *Id.* § 1395w-3a(c)(1).
95. *Id.* § 1395r-8(b)(3); *see also* Consolidated Appropriations Act, 2021, Pub. L. No. 116-260, div. CC, tit. 4, § 401, 134 Stat. 1,182, 2,995 (2020).
96. Ctrs. for Medicare & Medicaid Servs., *Medicare Claims Processing Manual*, ch. 17, § 20.1.2, https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c17.pdf (updated Dec. 2, 2021).
97. 42 U.S.C. § 1395w-3a(b); 42 C.F.R. § 414.904. In recent years, this has been adjusted to 104.3% of ASP, due to an across-the-board 2% decrease resulting from the application of sequestration. This 2% reduction was applied to all Medicare claims, after determining any beneficiary copayments. Thus, beneficiaries are still required to pay 80% of the ASP+6 rate. *See* Budget Control Act of 2011, Pub. L. No. 112-25, § 302, 125 Stat. 240, 256, 258–59 (2011). This sequestration reduction was put on hold during the COVID-19 pandemic.
98. 42 U.S.C. § 1395*l*(a)(1).
99. 42 C.F.R. § 419.2(b); Ctrs. for Medicare & Medicaid Servs., *Medicare Claims Processing Manual*, ch. 17, § 20.1.3, https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c17.pdf (last updated Dec. 2, 2021).
100. 42 U.S.C. § 1395w-3a(c)(4).
101. *See* Sustaining Excellence in Medicaid Act of 2019, Pub. L. No. 116-39, § 6, 133 Stat. 1061, 1062 (2019).
102. Ctrs. for Medicare & Medicaid Servs., *Medicare Claims Processing Manual,* ch. 17, § 10, https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c17.pdf (last updated Dec. 2, 2021).
103. 42 U.S.C. § 1395u(o)(1)(C); 84 Fed. Reg. 61,142, 61,145 (Nov. 12, 2019). The reimbursement rate of ASP minus 22.5% for 340B-acquired Part B drugs is currently being challenged in federal court. *See American Hosp. Ass'n v. Azar*, 967 F.3d 818 (D.C. Cir. 2020), cert granted, 141 S. Ct. 2883 (July 2, 2021). The Court heard oral arguments on the case on November 30, 2021. In 2020, CMS proposed, but did not finalize, a reimbursement rate of ASP minus 28.7% for 340B-acquired Part B drugs for CY 2021. 85 Fed. Reg. 48772, 48775 (Aug. 12, 2020).
104. 42 U.S.C. § 1395w-23; 42 C.F.R. § 422.304.
105. 42 C.F.R. § 422.304(b).
106. 42 U.S.C. § 1395w-102(a).
107. 42 C.F.R. § 423.104.
108. The Patient Protection and Affordable Care Act, Pub. L. No. 111-148, §§ 3301-3315, 124 Stat. 119, 461-80 (2010).
109. For brand-name drug products purchased by beneficiaries in the coverage gap, manufacturers provide a 70% discount and Medicare pays an additional 5%. For generic drug products, Medicare pays 75% of the cost. Ctrs. for Medicare & Medicaid Servs., *2020 Medicare Advantage and Part D Advance Notice Part 2 and Draft Call Letter* (Jan. 30, 2019), https://www.cms.gov/Medicare/Health-Plans/MedicareAdvtgSpecRateStats/Downloads/Advance2020Part2.pdf.
110. Cong. Research Serv., Medicare Part D Prescription Drug Benefit 29 (updated Dec. 18, 2020).

111. 42 U.S.C. § 1395w-114.
112. *See* Ctrs. for Medicare & Medicaid Servs., *Announcement of Calendar Year (CY) 2023 Medicare Advantage (MA) Capitation Rates and Part C and Part D Payment Policies* (Apr. 4, 2022), https://www.cms.gov/files/document/2023-announcement.pdf.
113. Medicare Payment Advisory Comm'n, *Report to Congress: Medicare Payment Policy* 472 (Mar. 2022), https://www.medpac.gov/wp-content/uploads/2022/03/Mar22_MedPAC_ReportToCongress_SEC.pdf.
114. 42 U.S.C. § 1395w-115.
115. Cong. Research Serv., R40611, Medicare Part D Prescription Drug Benefit (2018).
116. 42 U.S.C. § 1395w-111(i). Recent legislative efforts, such as President Biden's Build Back Better legislative proposal and other bills introduced in Congress, propose allowing the HHS Secretary to negotiate or establish a program to allow Medicare to negotiate certain drug products that pose the highest costs to Medicare. *See* Build Back Better Act, H.R. 5376, 117th Cong. § 1191 (2021); Elijah J. Cummings Lower Drug Costs Now Act, H.R. 3, 116th Cong. (2019).
117. Medicare Payment Advisory Comm'n, *Part D Payment System* 3 (2021), https://www.medpac.gov/wp-content/uploads/2021/11/medpac_payment_basics_21_partd_final_sec.pdf.
118. Social Security Amendments of 1965, Pub. L. No. 89-97, tit. XIX, 79 Stat. 286, 343–53 (1965).
119. 42 U.S.C. § 1396a.
120. *Id.* § 1396a(a)(10). Other statutes and regulations promulgated by CMS also defined eligibility pathways. *See, e.g.*, *id.* § 1396v; 42 C.F.R. Part 435.
121. 42 U.S.C. §§ 1396b(m), 1395mm(a)(1).
122. *Id.* §§ 1396a, 1396u-7.
123. *Id.* §§ 1396a(a)(54), 1396u-7(b)(2)(A).
124. *See Medicaid Benefits: Over-the-Counter Products*, Kaiser Family Found., https://www.kff.org/other/state-indicator/medicaid-benefits-over-the-counter-products/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D (last visited Apr. 12, 2022).
125. 42 U.S.C. § 1396u-5(d)(1).
126. *See generally id.* § 1396r-8.
127. In 2021, CMS approved a § 1115 demonstration waiver allowing Tennessee to adopt a closed formulary model. *See* Ctrs. for Medicare and Meicaid Servs., *CMS Approves Innovative Tennessee Aggregate Cap Demonstration to Prioritize Accountability for Value and Outcomes*, (Jan. 8, 2021), https://www.cms.gov/newsroom/press-releases/cms-approves-innovative-tennessee-aggregate-cap-demonstration-prioritize-accountability-value-and.
128. 42 U.S.C. § 1396r-8(a)-(b).
129. *Id.* § 1396r-8(d)(2).
130. 42 C.F.R. § 447.53.
131. Medicaid Program: Covered Outpatient Drugs, 81 Fed. Reg. 5,169, 5,174-76, 5,347 (Feb. 1, 2016) (codified at 42 C.F.R. § 447.502) (replacing the estimated acquisition cost ("EAC") with AAC).
132. *Id*. at 5176.
133. 42 C.F.R. § 447.502.
134. 42 U.S.C. § 1396a(a)(30)(A).
135. Medicaid & CHIP Payment & Access Comm'n, *Medicaid Payment for Outpatient*

Prescription Drugs 6 (May 2018), https://www.macpac.gov/wp-content/uploads/2015/09/Medicaid-Payment-for-Outpatient-Prescription-Drugs.pdf.

136. Rachel Dolan, *Understanding the Medicaid Prescription Drug Rebate Program*, Kaiser Family Found. (Nov. 12, 2019), https://www.kff.org/medicaid/issue-brief/understanding-the-medicaid-prescription-drug-rebate-program/.
137. *See, e.g.*, Wis. Stat. Ann. § 632.865(7); La. Stat. Ann. § 22:1657.1.C (1)(a)-(d).
138. The Massachusetts Attorney General's Office has been engaged in an ongoing review of various PBM's drug pricing practices, and it has reached settlements with several entities for drug pricing violations, including OptumRx, Walgreens, Stop & Shop, and United Pharmacy. *See* Office of Attorney General Maura Healey, *Optum Rx to Pay $5.8 Million for Alleged Failure to Follow Workers' Compensation Prescription Pricing Procedures*, (Feb. 24, 2022), https://www.mass.gov/news/optum-rx-to-pay-58-million-for-alleged-failure-to-follow-workers-compensation-prescription-pricing-procedures; *see also* Anna Wilde Mathews, *States Probe Business Practices of Pharmacy Benefit Managers*, Wall. St. J. (May 11, 2021), https://www.wsj.com/articles/states-probe-business-practices-of-pharmacy-benefit-managers-11620730804 (noting that seven states and Washington D.C. have announced investigations into PBMs). In addition, in 2020, the Ohio state auditor released a report finding that state PBMs collected $208 million in fees for generic Medicaid prescriptions paid my managed care plans between April 1, 2017 and March 31, 2018. *See* Ohio Auditor of State, *Ohio's Medicaid Managed Care Pharmacy Services* 2 (Aug. 16, 2018), https://ohioauditor.gov/auditsearch/Reports/2018/Medicaid_Pharmacy_Services_2018_Franklin.pdf.
139. *See, e.g.,* Complaint, *Ohio Highway Patrol Retirement Sys. v. Express Scripts, Inc.*, No. 20CV004504 (Ohio Com. Pl. July 13, 2020).
140. *See* 42 U.S.C. § 1396r-8(e)(4).
141. *See id.* § 1396r-8(e)(5); 42 C.F.R. § 447.514. If the FUL is less than the average AAC for retail community pharmacies, FUL is calculated using a higher multiplier to reflect average retail community pharmacies' acquisition costs. 42 C.F.R. § 447.514.
142. Cong. Research Serv., R43778, Medicaid Prescription Drug Pricing and Policy 13 (2014).
143. 42 C.F.R. § 447.512(b).
144. 42 U.S.C. § 1396r-8(b).
145. *Id.* § 1396r-8(c).
146. Medicaid Program; Establishing Minimum Standards in Medicaid State Drug Utilization Review (DUR) and Supporting Value-Based Purchasing (VBP) for Drugs Covered in Medicaid, Revising Medicaid Drug Rebate and Third Party Liability (TPL) Requirements, 85 Fed. Reg. 87,000 (Dec. 31, 2020) (to be codified at 42 C.F.R. § 447.502). In addition, the 2020 final rule expanded the "new formulations" subject to the line extension alternative rebate, to account for any change to the drug, including, but not limited to, an extended release formulation or other change in release mechanism, or change in dosage form, strength, route of administration, or ingredients. *Id.* at 87,034. To apply the line extension alternative rebate, only the initial single source drug or innovator multiple source drug must be an oral solid dosage form. *Id.* at 87,033. Additionally, the rule redefined "solid oral dosage form" more broadly than the long-standing FDA and CMS definitions to include any "orally administered dosage form that is not a liquid or gas at the time the drug enters the oral cavity." *Id.* at 87,044, 87,102. Finally, the rule instructs manufacturers to evaluate the rebate for each drug in their line extension family on a quarterly basis. *Id.* at 87,003.

As mentioned above, the drug with the highest additional rebate should be used to determine the alternative rebate.

147. Developed from Cong. Research Serv., R43778, *supra* note 134, at 17 (definitions omitted).
148. CPI-U is the consumer price index for all urban consumers as updated by the U.S. Department of Labor.
149. The 340B program was established in 1992 through section 340B of the Public Health Services Act. *See* Veterans Health Care Act of 1992, Pub. L. No. 102-585, § 602, 106 Stat. 4943, 4967-71 (1992) (enacting Section 340B of the Public Health Service Act). 340B is administered by Health Resources and Services Administration ("HRSA"), an agency within HHS, through HRSA's Office of Pharmacy Affairs ("OPA"), and effectuated through the Pharmaceutical Pricing Agreement and addendum (collectively "PPA").
150. Mike McCaughan, *The 340B Drug Discount Program*, Health Affairs (Sept. 14, 2017), https://www.healthaffairs.org/do/10.1377/hpb20171024.663441/full/.
151. 42 U.S.C. § 256b.
152. *See e.g.*, Rena M. Conti & Peter B. Bach, *The 340B Drug Discount Program: Hospitals Generate Profits By Expanding To Reach More Affluent Communities*, Health Affairs (Oct. 2014), https://www.healthaffairs.org/doi/10.1377/hlthaff.2014.0540.
153. Pub. L. No. 111-148, § 7101, 124 Stat. 119, 821-22 (2010); Notice Regarding 340B Drug Pricing Program—Contract Pharmacy Services, 75 Fed. Reg. 10,272 (Mar. 5, 2010); Stephen Barlas, *Health Care Reform Bill Expands Access to Section 340B Discounted Drugs for Hospitals*, 35 Pharmacy & Therapeutics 632, 632–34 (2010).
154. Avalere, *Hospital Acquisitions of Physician Practices and the 340B Program* 4 (June 2015), https://avalere.com/insights/avalere-white-paper-hospital-acquisitions-of-physician-practices-and-the-340b-program.
155. Adam J. Fine, *Exclusive: 340B Program Purchases Reach $24.3 Billion—7%+ of the Pharma Market—As Hospital Charity Care Flatlines*, Drug Channels (May 14, 2019), https://www.drugchannels.net/2019/05/exclusive-340b-program-purchases-reach.html; Adam J. Fine, *Exclusive: 340B Program Hits $16.2 Billion in 2016; Now 5% of U.S. Drug Market*, Drug Channels (May 18, 2017), https://www.drugchannels.net/2017/05/exclusive-340b-program-hits-162-billion.html.
156. Medicare Program: Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs, 82 Fed. Reg. 52,356, 52,362 (Nov. 13, 2017) (effective Jan. 1, 2018).
157. *American Hosp. Ass'n v. Azar*, 385 F. Supp. 3d. 1 (D.D.C. 2019).
158. Michelle M. Stein, *Hospitals Ask Supreme Court To Take Up 340B*, *Site Neutral Pay Cuts*, InsideHealthPolicy (Feb. 11, 2021; 12:57 PM ET), https://insidehealthpolicy.com/inside-drug-pricing-daily-news/hospitals-ask-supreme-court-take-340b-site-neutral-pay-cuts.
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* * *

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