

Paradigms and perspectives

Cost considerations for clinicians prescribing biologic drugs: Who pays?

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Biologic drugs for difficult-to-treat asthma are expensive, giving rise to complex systems of payment schemes. In turn, health plans rely on pharmacy benefit managers (PBMs) to create health plan formularies and administer drug benefit claims. This article describes a case and then highlights the payment process with a focus on the role of PBMs.

A 42-year-old woman with poorly controlled asthma has experienced multiple asthma exacerbations in the past year despite adherence to guideline-based maximum medical therapy. She requires oral corticosteroids to achieve asthma control. An attempt to address modifiable risk factors for uncontrolled asthma is unsuccessful. Her physician decides to prescribe a biologic drug and completes a prior authorization, which is sent to a PBM working on behalf of her health insurance company. The PBM denies coverage because the prior authorization did not meet all health plan criteria. While the physician submits an appeal, the patient experiences an asthma-related hospitalization. One month later, the biologic drug is approved. The patient's specialty pharmacy tells her the co-payment is \$1000 monthly, but she is unable to afford it.

In the United States, access to biologic drugs for asthma is limited because of high prices. Table I lists the average wholesale price, or reference price, for these drugs. Delivering specialty drugs to the health care marketplace has resulted in the formation of complex payment systems with multiple intermediaries, including PBMs, and rising administrative costs.¹ Generally, administrative costs of specialty drugs burden all stakeholders: pharmaceutical manufacturers, health insurance plans, PBMs, plan sponsors (eg, employers or government), health care providers, and beneficiaries. However, who pays and who profits from this process is not transparent. The average wholesale price is a good estimate of the cash-only price and is available to patients and clinicians, but does not accurately reflect the acquisition price for pharmacies or insurance companies.

Insurance plans provide patients with financial access to prescription drugs in the United States. Private insurance is delivered through group commercial, employer-based, and individual plans. Public insurance includes Medicare and Medicaid. Medicare is provided by the federal government to beneficiaries who meet specific requirements, such as age, and is funded through federal tax dollars. Medicare Part D is facilitated by PBMs for additional coverage of prescription drugs. Patients contribute to the payment of the Part D plan through cost sharing and premiums. Medicaid is provided for low-income individuals, with limited cost sharing for patients. It is funded by state and federal government tax dollars, but is administered by the states. The type of insurance is important because availability and cost for specialty asthma biologic drugs vary by insurance plan.

Fig 1² outlines the communication between stakeholders in the outpatient specialty prescription reimbursement process. Health insurance companies first negotiate with plan sponsors and then negotiate reimbursement rates, provide payment for care, and approve or disapprove services.³ The burden of cost eventually falls to the sponsor and beneficiary through risk pooling contractual agreements and higher premiums.⁴

Health insurance companies partner with PBMs to manage pharmaceutical costs by negotiating with buyers, including employers, union plans, government purchasers, and distributors of pharmaceuticals.¹ PBMs are at the center of the reimbursement process (Fig 1). They were originally established in the late 1960s to help health plans control pharmaceutical costs.² PBMs have evolved into industry giants, acquiring pharmacies and integrating with health insurance companies. PBMs are the principal purchaser of drugs in the United States and report an average consumer claim cost savings of \$941 per year achieved through different management tools.¹ However, PBMs have recently faced criticism over rising drug prices.¹

PBMs mitigate costs for health insurance companies by limiting access to expensive drugs.⁴ Tools used to accomplish this include formularies; step therapy, in which a preferred drug must be used before a nonpreferred drug; prior authorizations; indication restrictions; and higher cost-sharing tiers, in which patient out-of-pocket cost increases as the formulary tier increases.² PBMs restrict market access to specialty drugs by limiting medication dispensation and filling to designated PBM-contracted or PBM-owned specialty pharmacies.⁴

PBMs also use spread pricing, clawbacks, and rebates to increase profits. Spread pricing entails charging more money to the plan sponsor than is reimbursed to a pharmacy for the same medication.⁴ Clawbacks occur when PBMs charge co-payments that exceed the cost of acquisition of a drug.⁴ This difference in price was initially hidden because of the presence of "gag-clauses" between pharmacies and PBMs that prevented a pharmacy from disclosing the cost of a drug to a patient. Because of recent legislation, gag-clauses are no longer permitted. These methods are used to increase

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TABLE I. Who pays? This table compares how much a patient without insurance would pay estimated by the annual average wholesale price (AWP), compared to a patient on Medicare. Commercial insurance is variable but the patient may pay very little out of pocket. How much a patient on Medicaid pays varies by state.

Annual AWP* of an asthma biologic drug for a 70-kg adult male					Medicare Part D asthma biologic drug patient-out-of-pocket cost estimation 2020				
	Benralizumab	Mepolizumab	Omalizumab	Dupilumab	Month	Benralizumab	Mepolizumab	Omalizumab	Dupilumab
Dose	30 mg monthly for 3 doses, then every 8 wk	100 mg/mo	300 mg/mo	600 mg load, then 300 mg every other week	January	\$1,408.70	\$1,154.03†	\$907.22‡	\$1,050.04‡
					Deductible met and coverage gap phase reached				
					February	—	\$827.78	\$580.97	\$723.80
					March	\$1,082.45	\$701.69	\$580.96	\$723.79
					Catastrophic coverage phase reached				
					April	—	\$165.56	\$580.96	\$268.24
					Catastrophic coverage phase reached				
					May	\$160.82	\$165.56	\$117.69	\$144.76
					June	—	\$165.56	\$116.19	\$144.76
					July	\$216.49	\$165.56	\$116.19	\$144.76
					August	—	\$165.56	\$116.19	\$144.76
					September	\$216.49	\$165.56	\$116.19	\$144.76
					October	—	\$165.56	\$116.19	\$144.76
					November	\$216.49	\$165.56	\$116.19	\$144.76
					December	—	\$165.56	\$116.19	\$144.76
Annual	\$39,917.71 year 1	\$43,480.80	\$41,669.10	\$43,500.12	Annual	\$3,517.93‡	\$4,173.54	\$3,581.13	\$4,068.71‡
out-of-pocket cost	\$34,215.18 thereafter				out-of-pocket cost	\$3,301.44§			\$3,923.95§

AWP, Average wholesale price; IV, intravenous. This table provides an estimation of AWP and estimations of monthly and annual out-of-pocket costs for a Medicare Part D patient for each of the different asthma biologic drugs. **For commercially insured patients, the co-payment will vary on the basis of plan specifics, but it can range from \$0 to the full AWP cost of medications depending on deductibles and coinsurances.** The dosing is as follows: Fasenna (benralizumab) 30 mg every other month, Nucala (mepolizumab) 100 mg every month, Xolair (omalizumab) 300 mg every month, and Dupixent (dupilumab) 300 mg every 2 wk. This is an estimation because the cost of the drug may vary throughout the year, other prescribed medications will change time and duration of coverage phases for patients, and because plan specifics (such as premiums) will vary for different patients. Reslizumab was not included as an estimation for a Medicare Part D patient because it is administered via IV infusion and is not reimbursable as a prescription benefit. This table was adapted from [Medicare.gov](https://www.medicare.gov) price estimator with the parameters of the patient's plan: having a \$435 annual deductible, \$0 monthly premium, and 25% initial and coverage gap coinsurance. The annual out-of-pocket cost is an estimation and may vary per plan. Fasenna and Dupixent both have a loading dose, which will subsequently result in a more expensive annual cost for the first year of therapy. Xolair was estimated with a 300 mg monthly dose, but may be more expensive or less expensive depending on patient's weight and IgE level at the time of initiation of therapy. For instance, a patient receiving Xolair 375 mg every 2 wk would have an estimated annual out-of-pocket cost of \$6527.58.

*AWP is the average value at which wholesalers sell drugs to physicians, pharmacies, and other customers. AWP is a generally accepted standard measure for calculating the cost of a medication. It is typically 20% greater than the value for which a manufacturer sells its products to distributors and large customers.

†First month accounts for 25% coinsurance and deductible.

‡Annual estimation of price for initiation of therapy to account for loading dose.

§Annual estimation of price for maintenance dosing.

Insurance and Pharmacy Benefit Manager Cycle

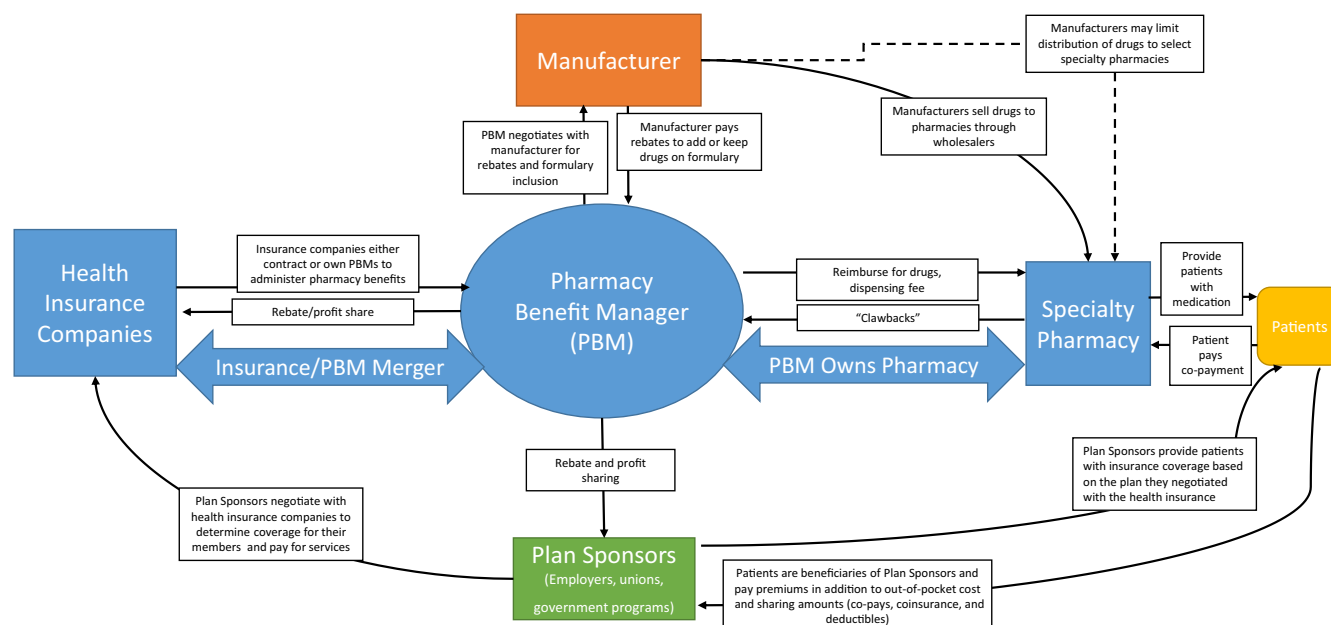


FIG 1. Insurance and PBM cycle. Who pays? We depict the central role of the PBM in the flow of drugs and money that results in payment of specialty drugs such as biologics. There are 3 large PBMs that in 2017 accounted for 73% of PBM market share and flow depicted in Fig 1. These PBMs are CVS Caremark, Optum, and Express Scripts. Each PBM owns its own specialty pharmacy: CVS Specialty Pharmacy, Briova, and Accredo, respectively. In addition, since 2016 there has been a merger of insurance companies and PBMs and now each of these PBMs is integrated with a health insurance company, resulting in the following relationship: Aetna and CVS Caremark, United Healthcare and Optum, Cigna and Express Scripts.⁵ The large arrow further demonstrates these relationships and the control now leveraged on the industry. In this reimbursement process, PBMs' rebates and profit sharing are directed to sponsors, payers, and themselves. They are not received by patients. The rebate and profit sharing is not transparent and only indirect measures are available for assessing this amount. In 2016, \$144 billion was paid from pharmaceutical manufacturers to intermediaries in this system.²

profit for the PBM and health plan, but it is not transparent and is not passed on to the patient.⁴

Drug rebates are negotiated discounts between PBMs and pharmaceutical manufacturers.⁴ PBMs' market control incentivizes pharmaceutical manufacturers to provide rebates to ensure formulary inclusion. Manufacturers pay billions of dollars of rebates annually to PBMs and partially attribute rising drug prices to rebates, but this is denied by PBMs.⁴ The rebates are kept by PBMs or are passed to the health insurance company or plan sponsor, a process lacking transparency.^{4,6} Currently, 85% of the market is controlled by 3 PBMs: CVS Caremark, OptumRx, and Express Scripts.⁴

The high drug costs, complex nature of the reimbursement process, and high demand for these drugs has generated tension between health care providers and payers.⁶ Payers argue that PBM review tactics reduce provider variation and promote consistent care.⁶ Payers attribute population-based variations in provider care to outdated clinical knowledge, investigational uses, and financial incentives for individuals or institutions.⁶ The reason for tension may be secondary to the complex nature of the reimbursement process and the need to control cost and resources to optimize clinical care. Providers perceive these tools as a way to maximize profits for payers at the expense of quality and timely care for patients.⁶

Before considering a biologic drug for asthma, physicians must ensure that modifiable risk factors for uncontrolled asthma, such as poor adherence, incorrect inhaler technique, and comorbidities, have been addressed. The medications can be prescribed by any provider in the United States, but typically insurance requires that the provider be an asthma specialist for reimbursement. Clinically, limiting prescribing to specialists in the area of practice for these agents as in France and the United Kingdom makes sense given the complexity of the conditions; however, there is no regulatory restriction on prescribing in the United States.

Upon prescribing biologic drugs, providers must devote resources to accomplish drug approval, often using designated staff to manage prior authorizations and communicate with insurance companies and specialty pharmacies. Currently, the reported industry standard for processing new specialty medications is 2 to 3 weeks for large PBM-owned specialty pharmacies. The duration may be shortened if the appropriate insurance assessment is completed by providers, and if patients are educated on the reimbursement and access process at the time of prescribing. PBMs have many expenses, including employing clinicians to review the appropriateness of therapy. Pharmaceutical manufacturers attempt to avoid delays in processing medications by assisting with prior authorizations and insurance benefit

investigations and by offering financial and co-pay assistance programs.²

Commercial and public insurance plans have highly variable coverage options, formularies, and out-of-pocket expenses. Plans vary depending on premiums, co-payments (the fixed dollar amount for prescription drugs paid by the patient), coinsurance (the percentage of total prescription drug cost paid by the patient), and deductibles. Most commercially insured patients qualify for coupon cards offered by manufacturers. Once asthma biologic drugs are approved, most commercially insured patients pay out-of-pocket between \$0 and \$100 per month.

Medicare offers standard reimbursement, allowing easier estimation of costs. Medicare Part D has designated coverage phases that change as spending thresholds are reached: deductible, initial coverage, coverage gap, and catastrophic coverage. The deductible varies on the basis of the plan, but will not exceed \$435 for 2020.⁶ In this phase, the patient is responsible for 100% of medication costs. This demonstrates the need for clear communication to patients to explain the cost structure and reduce the risk of primary nonadherence. The initial coverage phase and coverage gap entail a 25% coinsurance for brand name drugs.^{6,7} The initial phase lasts until \$3820 is spent by the patient and the plan. Once this is met, they transition to the coverage gap. In the coverage gap, the federal government and the manufacturer pay the remaining 75%.⁶ After \$5100 is spent, patients enter the catastrophic coverage phase until the end of the calendar year. In this phase, the federal government pays 80% of expenditures and part D plans pay 15%, leaving the patient responsible for 5% of expenditures.⁶ Patients on asthma biologic drugs typically reach catastrophic coverage after 3 to 4 months, but the cost is still often prohibitive.⁶⁻⁸ Table I provides estimates of out-of-pocket cost for asthma biologic drugs for Medicare Part D in the calendar year 2020. Medicare Part B covers medical billing or “buy-and-bill” and is typically used by an office or infusion suite that is equipped to access and submit for reimbursement after buying the medication for administration. Patients are responsible for 20% of the cost of administration and medication. With supplemental Medigap plans F, G, M, or N, the cost to the patient is typically \$0. Without a supplemental plan, the cost may be unaffordable for many patients.

Medicaid plans are either managed Medicaid plans, where a health insurance plan acts as an intermediary, or are managed by the state. The Centers for Medicare and Medicaid lists included and excluded drugs for each state. In addition, the drug formularies for managed Medicaid are available online. Some asthma biologic drugs are normally covered, but will require necessary demonstration of clinical appropriateness through prior authorization and/or appeals. Once approved the medications will have little to no cost sharing for patients.

Returning to the question of “Who pays?” the answer for individuals depends on the type of insurance. In our case, not all information was successfully obtained by the insurance company, resulting in initial denial of the biologic drug. In this scenario, the co-payment was \$1000. This co-payment amount may have been the standard co-payment or the cost may have been due to an

unmet deductible or coinsurance. If the patient had commercial insurance, then a co-payment card could have been obtained from the manufacturer to mitigate the expensive co-payment. The scenario is commonly encountered in clinical practice and exemplifies the communication problems and need for clinician familiarity to avoid lapses or delays in initiation of therapy. The coverage of asthma biologic drugs is restricted as discussed, but the PBM coverage tools have become so burdensome that they may prevent offices from accessing care for appropriate patients.

The integration of health insurance and PBMs has potential to disrupt the current reimbursement model because it directly bundles organizations responsible for health and pharmacy expenses. This may result in health plans making long-term cost assessments for coverage of medications. This long-term assessment may determine that downstream health expenditures, such as hospital readmissions, may be reduced if upfront expenditures are paid for drugs. However, the integration of health plans, PBMs, and pharmacies may lead to higher prices for consumers and government.

The reimbursement problems presented are very complex. They require detailed considerations on the broad economic consequences that would result if the current model was disrupted and is beyond the scope of this article. For clinicians the only true short-term solution is to familiarize themselves and their offices with the current reimbursement process to efficiently navigate the complex reimbursement system. Importantly, analysis must include a judgment of whether the short- and long-term clinical benefits and adverse effects of biologic drugs result in improvement in patient health sufficiently to justify the expense and burden associated with these specialty medications and that use of other, much less costly treatments has been optimized before considering a biologic.

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