Assembly
California Legislature

ASSEMBLY COMMITTEE ON HEALTH
JIM WOOD, CHAIR
ASSEMBLYMEMBER, SECOND DISTRICT

INFORMATIONAL HEARING

Understanding the Pharmaceutical Supply Chain:
What is Driving Up the Cost of Drugs?

Monday, October 31, 2016
10:00 a.m. – 1:00 p.m.
State Capitol, Room 4202

BACKGROUND

The cost of prescription drugs keeps rising and consumers are feeling the pinch. A national telephone survey conducted by the **Consumer Reports** "Best Buy Drugs" in March 2016 revealed that three in 10 Americans (about 32 million) were hit with price hikes within the previous 12 months, costing consumers an average of $63 more for a drug they routinely take and a few paid $500 or more.[1] This trend is reinforced by a study published by the *Journal of the American Medical Association (JAMA)* in August 2016 which reported that almost a quarter of 648 respondents to a 2015 poll reported that they or another family member did not fill a prescription in the last year because of cost. Data on national health expenditures reveal a similar pattern of rising costs. For example, in 2013, the Centers for Medicare and Medicaid Services (CMS) reported a 3.6% increase in healthcare spending, reaching $2.9 trillion or $9,255 per person or 17.3% of the Gross Domestic Product (GDP). In 2014, the per capita national health expenditures was $9,523, reaching $3 trillion which is 17.5% of the GDP. According to CMS, the faster growth was primarily due to the coverage expansions under the Patient Protection and Affordable Care Act (ACA), particularly Medicaid and private health insurance. Figures for 2015 and beyond are even higher.

CMS's forecast summary indicates that for 2015-2025[2], health spending is projected to grow at an average rate of 5.8% per year (4.8% on a per capita basis), which is 1.3% faster than the growth in the GDP per year over this period. As a result, the health share of GDP is expected to rise from 17.5% in 2014 to 20.1% by 2025. As the initial impacts associated with the ACA's coverage expansions fade, growth in health spending is expected to respond to changes in economic growth, faster growth in medical prices, and population aging. By the end of the projection, federal, state, and local

[1] Consumer Reports, Is There a Cure for High Drug Prices? July 29, 2016, http://www.consumerreports.org/drugs/cure-for-high-drug-prices.
[2] *See* <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/Proj2015.pdf>

governments are projected to finance 47% of national health spending (from 45% in 2014). With respect to prescription drugs, spending is projected to have grown 8.1% in 2015 and to have reached $321.9 billion, after a growth of 12.2% in 2014. CMS points out that this somewhat slower, but still relatively strong growth, is a result of the continued impact of newly approved and expensive drugs to treat conditions such as the hepatitis C virus (HCV) and cancer. Prescription drug spending is projected to grow an average of 6.7% per year for 2016 through 2025 as the influence on spending from newly approved drugs is expected to fade after two years of above average impacts. The point at which drug spending growth is projected to peak during the 10 year projection period is 2018; relatively fewer brand-name drugs are expected to lose patent protection and thus downward price pressure typically associated with the introduction of generic substitutes is somewhat mitigated.

Recent Drug Price Increases

Recent press and government action have highlighted the high pharmaceutical prices and increased prescription drug spending. For example, Mylan, which nearly owns the auto-injector market with its Food and Drug Administration (FDA)-approved Epinephrine Auto-Injector (EpiPen), faced scrutiny from the U.S. government for charging upwards of $600 for a two-pack set of EpiPens. In 2007, the price was $94. A September 2016 Kaiser Health Tracking Poll found that in the wake of the news about the increase in cost for the EpiPen, the majority (77%) of Americans say prescription drug costs are unreasonable, up slightly from 72% a year ago.

Another example of a recent prescription drug increase is Sovaldi. In December 2013, the FDA approved the drug produced by Gilead Sciences for the treatment of HCV. Sovaldi is represented as a significant advancement in HCV treatment as it provides a higher cure rate, allows for a shorter duration of treatment, has fewer adverse side effects, and opens up treatment options for individuals with comorbid conditions for which traditional treatments are contraindicated. While the drug has been found to be remarkably effective (curing 90% or more patients over the course of 12 weeks, according to the FDA), Gilead Sciences has come under heavy fire for initially pricing Sovaldi in the U.S. at $1,000 per pill ($84,000 for a 12 week treatment). Critics have raised additional concerns due to variation in costs globally. According to an April 2014 article in the *San Francisco Chronicle*, Gilead prices the treatment at $57,000 in the United Kingdom, $66,000 in Germany, while in Egypt and other developing countries the treatment costs $900, which is 99% less than the U.S. cost[3].

In addition to increases in the price of brand-name prescription drugs, there are reports highlighting the increase in the costs of some older generic drugs. The U.S. Government Accountability Office (GAO) found, in its examination of price trends for generic drugs and the factors that affect prices under Medicare Part D, that generic drug prices fell 59% from the first quarter of 2010 through the second quarter of 2015[4]. The GAO also found more than 300 out of the 1,441 established generic drugs that had at least one extraordinary price increase of 100% or more between first quarter 2010 and first

[3] *See* Stephanie M. Lee, *Cost of Gilead's Hepatitis C Pill, Sovaldi, Spurs Revolt*, SF Gate, April 13, 2014 http://www.sfgate.com/health/article/Cost-of-Gilead-s-hepatitis-C-pill-Sovaldi-spurs-5398315.php.
[4] *See* Generic Drugs under Medicare, GAO-16-706 (August 2016) http://www.gao.gov/assets/680/679022.pdf.

quarter 2015. The GAO determined that the drugs with extraordinary price increases moderated the overall decline in generic drug prices. Generic manufacturers reported that competition, determined by the price and availability of the same drug from other manufacturers, is the primary driver of generic drug prices, as less competition could drive prices higher.

Recent Lawsuits and News

In September 2016, Attorney General Kamala D. Harris announced that California, along with 34 other states and the District of Columbia, have filed lawsuits against Indivior, a British pharmaceutical company, and MonoSol RX, an Indiana pharmaceutical film technology company, for antitrust violations. The complaint, filed in U.S. District Court for the Eastern District of Pennsylvania, alleges that Indivior and MonoSol RX engaged in a multi-pronged "product-hopping" scheme to block competition to Suboxone, an opioid addiction treatment, ultimately generating almost $1 billion in undeserved profits. In this kind of scheme, pharmaceutical companies try to maintain profits generated through a monopoly by slightly reformulating their product in a way that blocks generic competitors without offering any significant medical or therapeutic advantages to patients. Additionally, the Orange County District Attorney announced recently that he has sued seven pharmaceutical companies for allegedly entering into a deal to artificially inflate the price of the cholesterol drug, Niaspan[5].

In early October, Senator Bernie Sanders called out Ariad Pharmaceuticals over the price of its leukemia drug Iclusig, and the company's stock dropped fast, by 15%. Ariad, which makes Iclusig, raised the price of the drug four times this year and now costs $199,000 a year, before factoring in insurance or any discounts. When it was first approved in 2012, the drug cost $9,580 a month. Now, it costs $16,560 a month, a 73% increase. Along the way, the drug has had some safety problems and actually got pulled off the market in 2013 by the FDA, but a few months later was reinstated with warnings about cardiovascular problems that may occur[6].

Recent publications have attempted to address the increases in prescription drug spending that have dominated the news as of late, identifying possible factors contributing to these increases, and describing how the complexity of the pharmaceutical supply system could be contributing to these price increases.

Factors Contributing to Drug Prices

Brand. According to a 2016 *JAMA* article[7] the primary reason for increasing drug spending is the high price of branded products protected by market exclusivity provisions granted by the U.S. Patent and

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[5] Kelly Puente, *O.C. District Attorney's Office sues drug companies for allegedly paying to delay launch of generic cholesterol drug*, Orange County Register, October 6, 2016 http://www.ocregister.com/articles/drug-731330-generic-pay.html.

[6] Lydia Ramsey, *Bernie Sanders just called out a drug company for jacking up the price of its leukemia drug — and the shares are tanking*, Business Insider, October 14, 2016 http://www.businessinsider.com/ariad-pharmaceuticals-stock-dropping-after-bernie-sanders-tweet-2016-10.

[7] Kesselheim AS, Avorn J, Sarpatwari A. *The High Cost of Prescription Drugs in the United State Origins and Prospects for Reform*, JOURNAL OF AMERICAN MEDICAL ASSOCIATION 858 (2016).

Trademark Office and the FDA. The *JAMA* article reported that although brand-name drugs comprise only 10% of all dispensed prescriptions in the U.S., they account for 72% of drug spending. The *JAMA* article cited to the annual cost of a growing number of "specialty drugs"–high-cost, often injectable biologic medications which can exceed $250,000 per patient. These drugs include eculizumab (Soliris - for the treatment of pediatric and adult patients with atypical hemolytic uremic syndrome), pralatrexate (Folotyn - for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma), and elosulfase alfa (Vimizim - the first FDA-approved treatment for Mucopolysaccharidosis Type IVA (Morquio A syndrome), a rare, autosomal recessive lysosomal storage disease caused by a deficiency in N-acetylgalactosamine-6-sulfate sulfatase). The *JAMA* article also stated that high prices have historically been limited to brand-name drugs that treat rare conditions, however, drugs that treat conditions affecting millions of individuals in the U.S. also now have high costs, like many new oncology drugs.

Generic. The *JAMA* article also stated that although brand-name drugs account for the greatest increase in prescription drug expenditures, another area that has captured the attention of the public and of policy makers is the sharp increase in the costs of some older generic drugs. In 2015, Turing Pharmaceuticals raised the price of pyrimethamine (trade name Daraprim), a 63-year-old treatment for toxoplasmosis, by 5,500%, from $13.50 to $750 for a single pill. The company was able to set the high price despite the absence of any patent protection because no other competing manufacturer was licensed to market the drug in the U.S. Significant increases in the prices of other older drugs include isoproterenol (2,500%) (for the treatment of bradycardia (slow heart rate), heart block, and rarely for asthma), nitroprusside (1,700%) (for the treatment of high blood pressure), and digoxin (637%) (for the treatment of various heart conditions, namely atrial fibrillation, atrial flutter and sometimes heart failure that cannot be controlled by other medication). Even though the prices of most generic drug products have remained stable between 2008 and 2015, those of almost 400 (approximately 2% of the sample investigated) increased by more than 1,000%.

Research and Development. Due to the complexity and length of time invested in research, it is difficult for analysts and researchers to assess exactly how much it costs to bring one drug to market. The timeframe of development can last for decades, and may be a combination of efforts from multiple companies or previous research on other drugs. A recent report released by the Tufts Center for the Study of Drug Development found that the average cost to research and develop a new medicine has doubled over the past decade to $2.6 billion. When the costs of post-approval research and development were factored in, the estimate increased to $2.8 billion[8]. One analysis of publicly available data performed by *Forbes* magazine in 2013 estimated the cost of bringing a drug to market can vary from $350 million to $4.5 billion[9]. The *JAMA* article identified the sales and research and development expenditures of the 10 largest pharmaceutical companies, ranking the top three as Novartis, spending $9943 million, Pfizer, $8393 million, and Sanofi, $5873 million in research and development costs.

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[8] DiMasi JA, Grabowski HG, Hansen RA. *Innovation in the pharmaceutical industry: new estimates of R&D costs*. JOURNAL OF HEALTH ECONOMICS 20 (2016).

[9] Matthew Herper, *The Cost of Creating a New Drug Now $5 Billion, Pushing Big Pharma To Change*, Forbes, August 11, 2013 http://www.forbes.com/sites/matthewherper/2013/08/11/how-the-staggering-cost-of-inventing-new-drugs-is-shaping-the-future-of-medicine/.

Role of Intermediaries or Middlemen. The *JAMA* article stated that in the 1990s, pharmacy benefit managers (PBMs) became prominent intermediaries whose role would be to help employers or insurers promote appropriate prescription drug use and decrease its cost. The *JAMA* article cited to recent isolated examples in which PBMs have decreased costs for specific drugs (most prominently for drugs treating HCV or the pro-protein convertase subtilisin/kexin type 9 inhibitors to reduce cholesterol levels). The *JAMA* article also stated aggressive price negotiation is not the norm but this is not surprising because part of PBMs' annual fees is based on a given payer's spending on drugs. Although the details of such payments are rarely disclosed, when one of the largest PBMs (Medco) became a publicly traded entity, it was obliged to disclose its business model, which revealed that much of its business depended on payments from drug makers for shifting market share to their products from others in its class.

With the rise in prescription drug pricing and PBMs such as Express Scripts and the pharmacy-benefit units of CVS Health and UnitedHealth Group reporting big profits, there are questions regarding PBMs' effectiveness[10]. After rising four times more than the market in the past decade, shares of Express Scripts were affected early this year when the company's largest commercial client, health-insurer Anthem, claimed in a lawsuit that Express Scripts was overcharging it by $3 billion a year. Express Scripts disputes the claim, and the stock has begun to recover. But analysts fear that it will lose Anthem's business and, with it, as much as 20% of its earnings. Additionally, in February of this year, 20 of the nation's largest corporations (including American Express Company, IBM Corporation, Macy's, and Verizon Communications Inc.) formed the Health Transformation Alliance. This alliance is focused on reforms to the supply chain that are designed to reduce redundancies and waste and together these companies seek to make the current multilayered supply chain more efficient. The Health Transformation Alliance, a not-for-profit entity, will lead the effort to transform the system and will serve as part of each company's health strategy, bringing increased innovation, better analyses of the latest data, and greater leverage into how corporations obtain coverage for their workers.

Other Factors. Beyond research and development costs, there are other business factors that manufacturers will take into account when determining the list price of a drug, including but not limited to marketing, sales, advertising, information technology, legal defense, and the cost of raw materials. A June 2016 California HealthCare Foundation's (CHCF) Issue Brief[11] contended that as a consequence of government benefits and restrictions, the favorable pricing for the Veterans Administration and Medicaid set the floor for the lowest prices that other purchasers may try to negotiate. Confounding this issue is the nondisclosure of net drug prices; purchasers have no method to calibrate the comparative value of the drugs they are purchasing since contracts remain confidential. Consequently, purchasers are prevented from comparison shopping net prices. The *JAMA* article also discussed the role of public and private payers during a drug's exclusivity period and the negotiating power of the payer as the primary counterweight against excessive pricing. This Committee will

[10] Bill Alpert, *Pharmacy Benefit Managers Under Pressure*, Barron's, July 23, 2016 http://www.barrons.com/articles/pharmacy-benefit-managers-under-fire-1469247082.
[11] Marge Ginsberg et al. *When the Price is Not Right: State Options on Prescription Drug Pricing*, CALIFORNIA HEALTH CARE FOUNDATION (2016).

discuss the role of each payer, including Medicare, Veterans Health Administration, Medi-Cal, and employer groups in later hearings.

Other Countries. According to the *JAMA* article, drug prices are higher in the U.S. than in the rest of the industrialized world because the U.S. health care system allows manufacturers to set their own price for a given product whereas other countries take a different approach because of their distinct health care system. For example, in countries with national health insurance systems, like Australia, Canada, Germany, and the United Kingdom, a delegated body negotiates drug prices or rejects coverage of products if the price demanded by the manufacturer is excessive compared to the benefit provided. Manufacturers may then decide to offer the drug at a lower price. In England and Wales, for example, the National Institute for Health and Care Excellence considers whether a new drug passes a cost-utility threshold, usually between £20,000 and £30,000 ($25,000-$40,000) per quality-adjusted life-year added—before recommending it for coverage by the National Health Service. Although prices can vary widely around the world and have also increased faster than member states' GDP, in recent years in Europe, U.S. drug prices per capita still substantially outpace those in other settings.

Pharmaceutical Supply Chain

A 2005 Kaiser Family Foundation publication (KFF publication) entitled "Follow the Pill: Understanding the U.S. Commercial Pharmaceutical Supply Chain," described the pharmaceutical supply chain as the means through which prescription medicines are delivered to patients. Highlights from the publication include a description of the industry segments:

> ***Pharmaceutical Manufacturers.*** Manufacturers are the source of the prescription drugs in the pharmaceutical supply chain. The pharmaceutical manufacturing industry is comprised of brand-name and generic drug manufacturers. Manufacturers manage the distribution of drugs from manufacturing facilities to drug wholesalers, and in some cases, directly to retail pharmacy chains, mail-order and specialty pharmacies, hospital chains, health plans, and government purchasers. Wholesale distributors are the manufacturers' largest purchasers and very few drugs are distributed directly to consumers.
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> ***Wholesale Distributors.*** Wholesale distributors purchase pharmaceutical products from manufacturers and distribute them to a variety of customers, including pharmacies, hospitals, and long-term care and other medical facilities. At the time of the KFF publication, the wholesale distribution industry has consolidated in the last 30 years, with the number of wholesale distributors in the U.S. declining from approximately 200 in 1975 to fewer than 50 in the year 2000. Combined, the three top drug wholesalers (McKesson, Cardinal Health, and AmerisourceBergen) handle more than 80% of all drugs distributed in the U.S. They provide drugs to retail pharmacy chains, independent pharmacies, hospitals, and nursing homes[12].

[12] *The Drug Wholesale Trade Goes All In, Yahoo Finance,* (December 27, 2013) http://finance.yahoo.com/news/drug-wholesale-trade-goes-213000416.html.

These wholesalers may facilitate discounts that are negotiated between manufacturers and other customers.

Pharmacies. Pharmacies are the final step on the pharmaceutical supply chain before drugs reach the consumer or patient. Pharmacies purchase drugs from wholesalers, and sometimes directly from manufacturers, and then take physical possession of the drug products and assume responsibility for their safe storage and dispensing to consumers. In addition to traditional retail pharmacy services, consumers have increasingly been using specialty and mail-order pharmacies over the past several years. Specialty pharmacies serve patients with chronic diseases by dispensing high-cost biotechnological drugs. Mail-order pharmacies receive prescriptions by mail, fax, phone, or the Internet at a central location; process the prescription in large, mostly automated centers; and, mail the prescribed drugs back to the consumer. Long-term care pharmacies, also called institutional pharmacies, address the special needs of nursing homes, providing packaging for controlled administration and special services that are more extensive than those provided by retail pharmacies (for example, quality assurance checks and emergency delivery services). Pharmacies may negotiate with manufacturers or wholesalers for discounts and rebates based on volume sales or market share, and they may negotiate with PBMs for inclusion in their networks and for their reimbursement.

Pharmacy Benefit Managers. PBMs have evolved from basic claims administrators to more complex organizations offering a wide range of prescription drug managed tools, like drug utilization review, disease management, and consultative services. PBMs can also assist clients with establishing their benefit structure, including developing and maintaining a prescription drug formulary; developing a network of pharmacy providers; and, providing mail order fulfillment services. PBMs may achieve savings for their customers by negotiating discounts and through cost containment programs, including use of formularies and cost sharing. In 2015, the three largest public PBMs were Express Scripts, CVS Health (formerly CVS Caremark), and United Health/OptumRx/Catamaran.

Financial Relationships in the Supply Chain. The KFF publication also addressed the flow of money and key financial relationships in the U.S. pharmaceutical supply chain. Most notably, the KFF publication stated the pricing of prescription drugs and the flow of money among the various links in the pharmaceutical supply chain is more complex than the physical distribution of drugs through the chain. This complexity can result in substantial variations in what different purchasers pay for the same drugs. The price of prescription drugs paid by the consumer is determined by an arrangement of negotiated contracts between manufacturers, PBMs, wholesale distributors, pharmacies, and plan sponsors. The price charged by each entity in the chain is largely driven by the ability of contracting entities to sell specific volumes of certain drugs or achieve a certain share of a specified market. It is also affected by the value each entity brings to the subsequent actors in the supply chain. Below are definitions to help understand the flow of money in the pharmaceutical supply chain:

Average Manufacturer Price (AMP). The average price paid to a manufacturer by wholesalers for drugs distributed to retail pharmacies. AMP was a benchmark created by Congress in 1990 in calculating Medicaid rebates and is not publicly available.

Average Sales Price (ASP). The weighted average of all non-Federal sales to wholesalers net of chargebacks, discounts, rebates, and other benefits tied to the purchase of the drug product, whether the ASP is paid to the wholesaler or the retailer.

Average Wholesale Price (AWP). Although not defined in statute, AWP is recognized as retail list price (sometimes referred to as a "sticker" price) and is currently used by some public and private third-party payers as the basis for reimbursement (e.g., AWP minus 5 or 25%). AWP has been widely criticized as a price that is: (1) not reflective of the true market price; and, (2) easily manipulated.

Estimated Acquisition Cost (EAC). EAC is a state Medicaid Agency's best estimate of the price generally paid by pharmacies for a particular drug.

Maximum Allowable Cost (MAC). MAC lists are designed to cap reimbursement for certain generic and multi-source brand products. States and private payers with MAC programs typically publish lists of selected generic and multi-source brand drugs along with the maximum price at which the program will reimburse for those drugs. In general, pharmacies will receive payment no higher than the MAC price when billing for drugs on a MAC list.

Wholesale Acquisition Cost (WAC). The price paid by a wholesaler for drugs purchased from the wholesaler's supplier, typically the manufacturer of the drug. Publicly disclosed or listed WAC amounts may not reflect all available discounts.

Purpose

In an effort to understand the factors that lead to unexpected drug price increases and offer meaningful solutions that assure patient access while controlling costs, this Committee will hold a series of informational hearings on prescription drug pricing. In this first hearing, the Committee will hear from experts who will provide a historical perspective on drug pricing, discuss the economics of drug pricing and drug pricing in other countries. An overview of the pharmaceutical supply chain will be provided and stakeholders, including manufacturers, wholesale distributors, PBMs and pharmacists will provide testimony on their roles in the supply chain. The subsequent hearings will explore the impact of prescription drug prices on the healthcare system and explore policy options that could contain costs while maintaining access.