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March 2023

US Pharmaceutical Market – Producers, Payers, Other Players

Horvath Health Policy, Innovations in Healthcare Financing

Laws, Regs, Barriers to Effective Policy

State Rx Policy

State Gov'ts Carry A Lot of Rx Costs

- State taxpayers typically fund some portion of pharmacy benefits for 25% **or more** of the state population.
  - Medicaid
  - State and Local Employee and their dependents
  - State and Local Retirees (with Medicare Part D)
  - State Corrections, Local Jails
  - State and Local Public Health
  - State Higher Education employees and student health services
- State tax expenditures for health insurance premiums, healthcare costs (as applicable, not all states)

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What States are Doing

- Transparency ☑ OR was 2nd state to enact,
  - Rx pricing, health plan Rx costs/spending, PBM reporting
  - Feds law follows state law.

☑ = lawsuit, OR= Oregon law

- Review state agency Rx procurements and PBM contracting (CA, WI, NM, MD, NJ) ☑ OR OHA
- Medicaid sole source contracting and pharmacy benefit budget caps (LA, WA, NY)
- Reworking Medicaid FFS PBM Contracts and Audits (WV, OH, NM, AL….)
- Maximizing access to 340B pricing ☑ industry v federal HHS
- Importation from Canada (VT, FL, CO, ME, NM) ☑
- Generic Manufacturing (CA, WA)
- Prescription Drug Affordability Boards/Upper Payment Limits (CO, MD, OR, MN)
- Extending Medicare Fair Price Statewide – all payers all purchasers (NV bill moving through legislature)
- State administered procurement & PBM services – OR Array Rx, MM Infuse
  - Array Rx pharmacy claims management and other services, administered by OR/WA open to public and private purchasers and payors in other states.
  - Market disruptor likely to get more uptake as disruption looks viable to more payors and purchasers
  - MM Infuse is GPO for any and all state and local govt entities – direct Rx purchasers, not payors/health insurers

PBM Laws

- Started in 2014 or earlier
  - Impetus: Independent pharmacies became collateral damage in market wars
  - Express Scripts announced in 2023 it will reimburse rural independents more that competitor chain pharmacies
  - PBM/retail pharmacy chain/specialty pharmacy (next slide)
  - Vertical integration has not helped consumers
    - 600 Rx no longer on the formularies of the big PBMs
- All manner of bad to egregious business behavior
  - Ex: CVS Caremark had volume-based rebate for a brand
    - Decided to move more market share and increase rebates
    - CVS retail stores only dispensed the brand for customers in its corporate orbit
- Whack-a-mole
  - States have to amend their laws over and over to keep up with evolving PBM business practices designed to skirt new laws
  - 1st step is to require licensure

How States are Hobbled in Addressing Rx Costs

- PhRMA has lots and lots of $$ to lobby and sue
  - States may not be resourced to fight pharma in court and thus decline significant action
- Whenever PhRMA/BIO sue it's an issue of constitutional law
  - Venue – get the lawsuit into federal court, which raises the costs and the stakes
- Constitutional Issues Raised by PhRMA Are Complex
  - Dormant Commerce Clause
  - ERISA law/Supremacy Clause
  - Patent Law/Supremacy Clause
  - FDA Law/Supremacy Clause
  - Trade Secrets/Supremacy Clause (also a state law issue)
  - Free Speech/1st Amendment
  - Cruel and unusual punishment/8th Amendment

Significant US Supreme Court Rulings

- Rutledge, 12/20
  - ERISA based challenge to AR PBM law regulating market behavior towrd pharmacy
  - *Unanimous* SCOTUS decision that state's have authority for healthcare rate setting – even if it costs ERISA plans money. (States still cannot impact ERISA benefit/covered services).
  - ERISA serves same function as Dormant Commerce Clause
    - Shields out of state/national/global companies from state level employee benefit regulation
- Pork Producers v. Ross 5/23
  - Complicated Dormant Commerce Clause decision finding that states can regulate commerce coming into state in areas feds have not regulated, where benefits to residents exceeds impact on interstate commerce.
- States can be bolder in their policy approaches

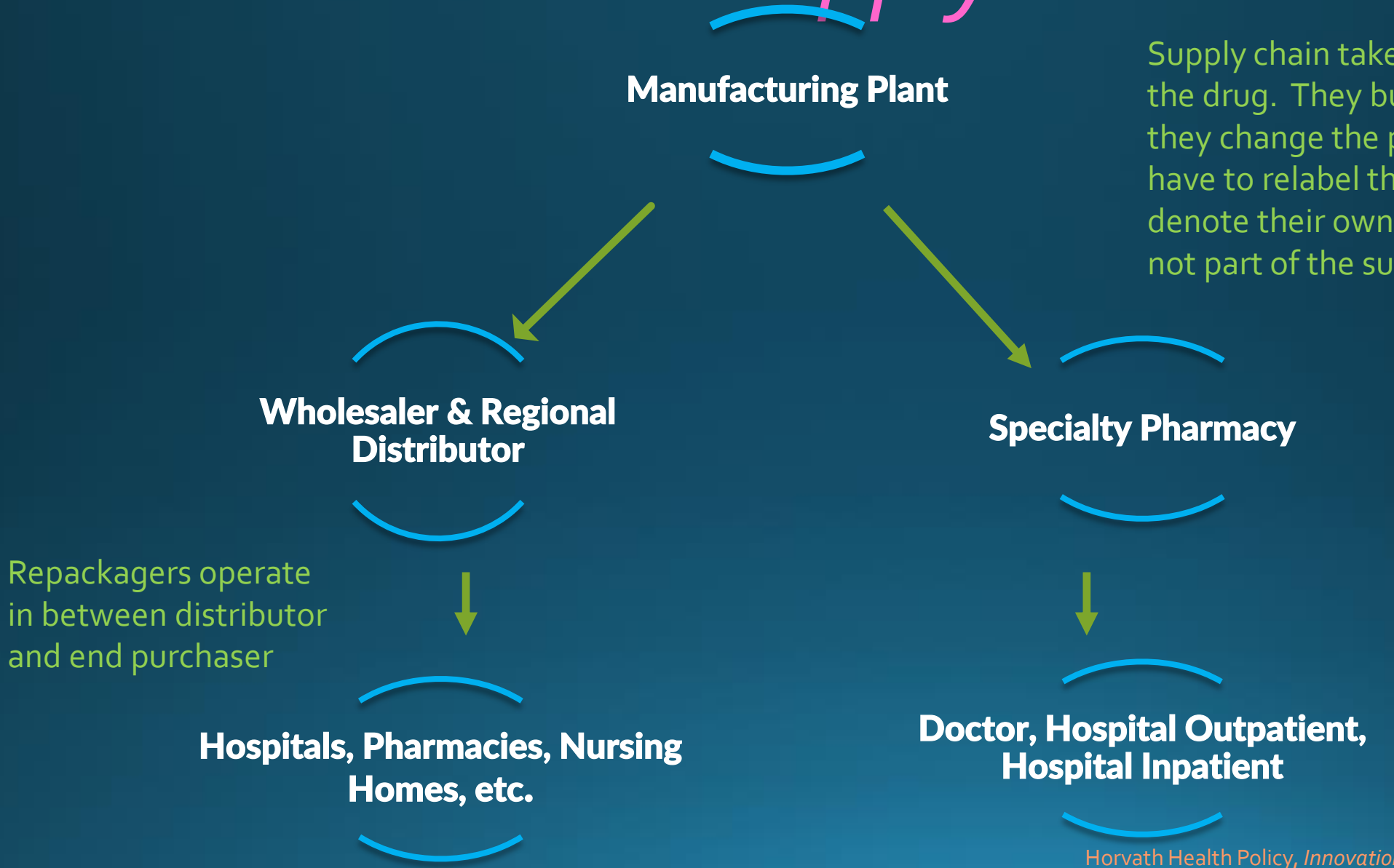
Market Players

Who, What, and Why

Rx Industry Legal and Regulatory Framework

- **Food and Drug Administration, Health and Human Services Department**
  - Licenses prescription drug products
    - New Drug Application (small molecule)
    - Abbreviated New Drug Application (AND, generics small molecule
    - Biologics License Application (large molecule, biologics and biosimilars)
  - Monitors Safety
    - Adverse Events Database
    - Sentinel System
    - Good Manufacturing Practices/physical plant inspections
  - Regulates Advertising
  - Wholesalers must also register
- **Centers for Medicaid and Medicare Services, HHS**
  - Drug Payment Amounts (Medicare Part B)
  - Anti kickback – Medicare and Medicaid (no drug-specific patient discounts or coupons…no inducement to use more services)
  - Coverage Policy (Medicare B and D)
  - Medicaid Drug Rebate Program
- **States license supply chain -- wholesaler to end purchasers (hospitals etc)**
  - Not all states regulate PBMs

Basics of Product *Supply* Chain



Supply chain takes ownership of the drug. They buy and sell. And if they change the packaging, they have to relabel the product to denote their ownership. PBMs are not part of the supply chain.

Who Does What? Manufacturers

- Bringing Drugs to Market
  - Buy promising molecules from research centers (Universities) that do the 'bench science'
  - Outright purchase price and/or contract for royalties if molecule is commercialized
  - Apply for patent (20 years) (or buy rights to the patent from original researcher)
  - Conduct R&D on molecules Phases 1-3/4 clinical trials – R&D to get Rx to market
  - Submit to FDA for approval
  - R&D to market can take 10 or 13 years, so 7-10 years left on the 20 year patent at FDA approva
  - Manufacturers are often state-licensed
- Set the price
  - Price may be set years before a drug reaches the market. Baked into company accounting so har change
- Can lease the drug license to another company to sell
- Sales and marketing, life cycle management
  - Price changes, price concessions, patient assistance

Who Does What? Wholesalers

- Buy in large quantity from manufacturers
- Store, Sell and Ship
  - to very large purchasers
  - to regional distributors (sometimes)
  - to pharmacies
    - Pharmacies may also have to register as wholesaler if a one site in a small chain stocks and distributes to the rest of the pharmacies in the company
- A wholesaler can have several roles
  - Specialty Pharmacy - McKesson administers the Vaccine for Children supply to pediatrician offices
  - Pharmacy Services Admin Org (PSAO) -- negotiates with manufacturers and PBMs on behalf of smaller pharmacies and provide administrative services

Who Does What? PBMs (or Insurers without PBM)

- Create pharmacy networks
  - Negotiate pharmacy professional (aka dispensing) fees
  - Set drug reimbursement amounts
  - Pay pharmacy claims, bill insurers for reimbursement
  - Operate mail order pharmacy (PBM only, not insurers)
- Operate formulary
  - Small plans take PBM national formularies, large plans may design their own
  - Negotiate manufacturer rebates based on formulary placement of drug(s)
  - Decides on pharmacy utilization management strategies for drugs
- Reimburse pharmacies and providers for drugs dispensed or administered to enrollees
- Collect manufacturer price concessions based on paid Rx claims (utilization)
- Not all states license PBMs

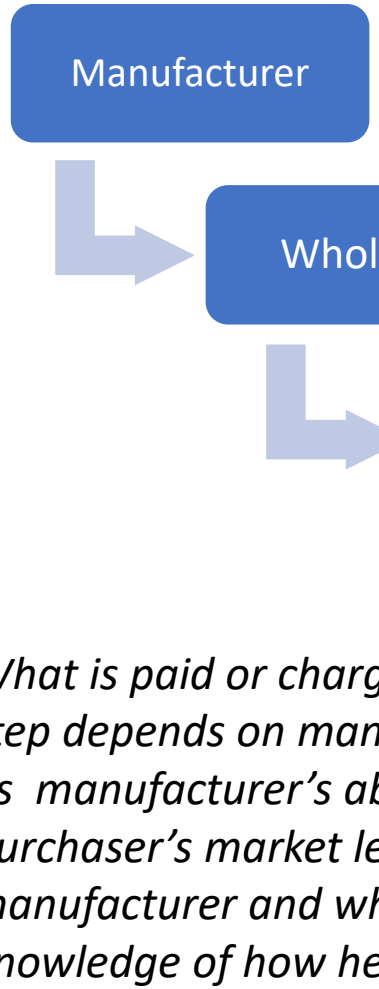
Who Does What? Insurers

- Contract with PBMs
  - Scope of PBM role depends on insurer, usually size of insurer
  - Reimburse PBM for pharmacy 'claims paid'
- Why contract with PBMs?
  - Running pharmacy benefit has become complex
    - Response to rising prices (utilization management)
    - Negotiate and managing manufacturer rebates
    - Need to negotiate with pharmacies and create networks
- Set overall premiums based on expected medical and pharmacy costs
  - Rx costs are increasing share of premium (23% or so)
- Run grievance and appeals for covered benefits
- Are state licensed (other than ERISA plans)

Who Does What? Pharmacies

- Retail pharmacies – open to public
  - Purchase drugs from wholesalers and distributors
  - Hire administrative services companies to handle claims wrangling and often group purchase negotiations (PSAOs, which can be wholesalers)
  - Counsel patients
  - Can't drive brand name market share but can drive generic market share
- Specialty pharmacies – may or may not also be retail pharmacies
  - Contract with manufacturers to handle specific, 'specialty' drugs
  - Work with administering providers to get product to offices as needed
  - Case management for patients on the drug
  - Administrative assistance to administering providers (handling, billing etc.)
  - Give manufacturers more control over distribution and ensure provider training, if needed

Basics of Rx Purchase Prices



Sets list price (WAC) & volume-based discount for wholesalers (WAC – discount). Negotiates on-invoice discounts with large healthcare entities.

Buys @ discount off the list price/WAC. Sells to pharmacies and hospitals at WAC minus but above what wholesaler paid (mark up). Also fulfills manufacturer discount agreements and gets reimbused from manufacturer .

Buys @ WAC minus. Bills PBM (submits a "claim") @ a mark up, close to list price.

Patient pays deductible, coinsurance or deductible based on what insurer/PBM will reimburse provider – close to WAC/list price.

PBM reimburses pharmacy @ Actual Acquisition Cost, often WAC plus or WAC minus. Negotiates and receives Rx rebates from manufacturers based on drug utilization. Bills insurers for pharmacy claims paid.

Contracts with PBM, may receive 100% of rebates from PBM, share rebates with PBM, or have PBM retain 100% of rebates. Reimburses PBM for its pharmacy payments.

What is paid or charged at each step depends on many factors such as manufacturer's ability to price, purchaser's market leverage, manufacturer and wholesaler knowledge of how health plans will reimburse.

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Vertical Integration

Corporate Relationships Focused on Maximizing Rebates

Source: Drug Channels 12/2022 https://www.drugchannels.net/

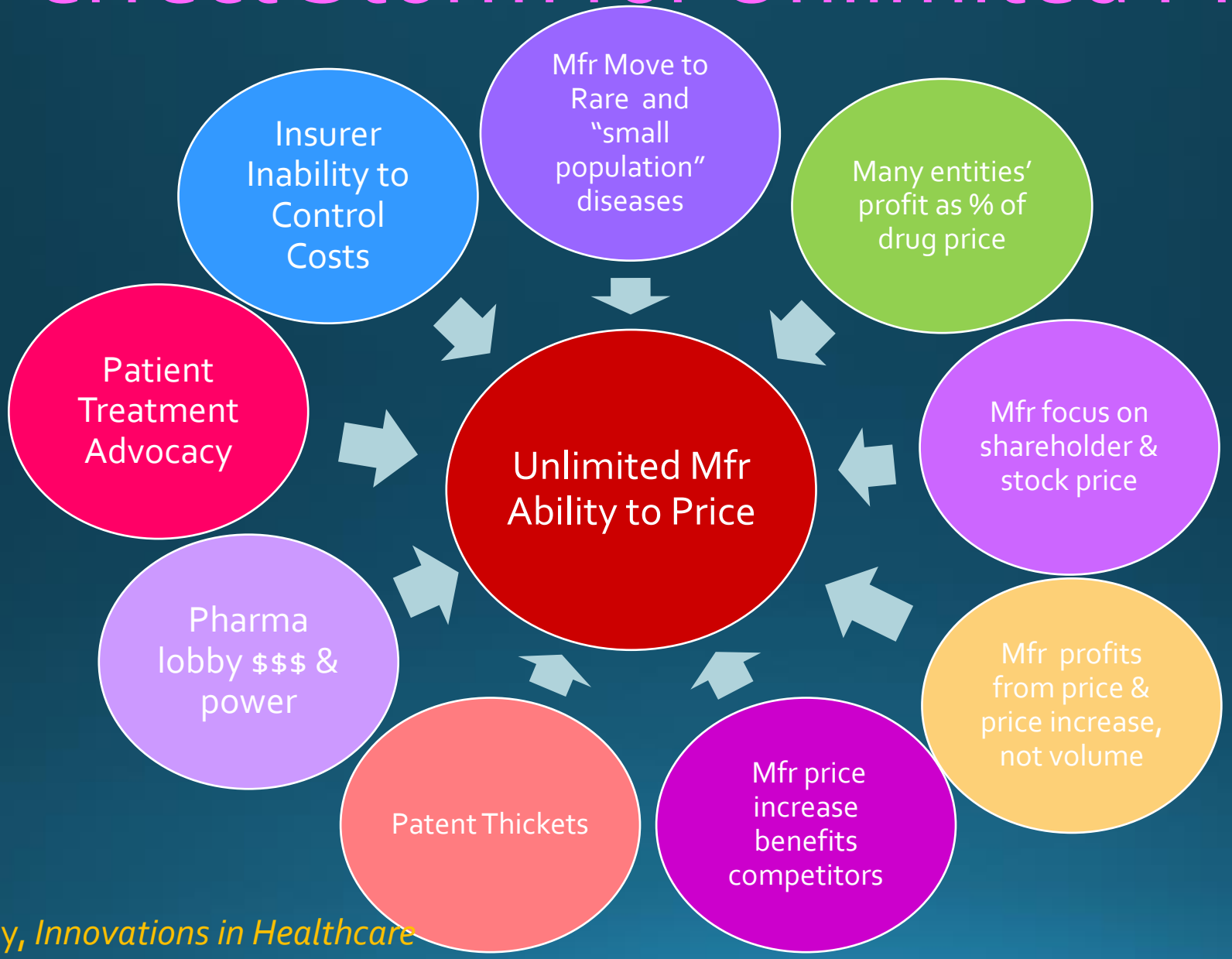
Rx Market – who's in the Fortune 100 in 2023?

Rx Manufacturers, Rank	Wholesalers, Rank	PBM/Pharmacy/Insurer, Rank
J&J, #37	McKesson, #9	CVS Health, #4
Humana, #40	Amerisource Bergen, #10	United Health Group, #5
Pfizer, #43	Cardinal Health, #15	Cigna, #12
Abbvie, #63		Walgreens Boots Alliance, #18
Merck, #71		Centene #26
BMS, #82		

How We Got Here

Pharma Long View

The Perfect Storm for Unlimited Pricing



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Industry Interest in Rare Disease <200000 people

- FDA designation of Orphan Drug Status confers
  - 7 years of exclusivity – no competition in disease state for *first drug*.
    - Additional drugs for same condition can get orphan status
  - FDA Rx development grants
  - Waiver of FDA $3.2M/drug application fee, and $400K annual/drug program fee
  - Expedited approvals (less clinical trial costs)
  - Tax credits up to 50% of clinical trial costs
- Orphan status never ends
  - Humira – was best selling Rx in the world, multiple orphan designations
  - Keytruda – soon to be global best seller, multiple orphan designations
- Orphan exclusivity is in addition to patent protection
  - but broader than patent --blocks off competition in the disease rather than mechanism of action
  - For biologic, orphan protection is in addition to 12 years of data protection and patent protection
- It's the new big focus
  - 1990, 87 orphan designations for approved and yet to be approved Rx
  - In 2022, 402 orphan designations for approved and yet to be approved Rx

Orphan Rx and Expedited Approval

- Shorter and smaller clinical trials, proxy endpoints
  - Reduces time and cost, and improves probability of approval
- Expedited Approval Pathways – unmet medical need
- Of the 37 novel new drugs approved in 2022 20 are orphan rx
  - Of 37 drugs 65% used 1 or more expedited approval pathways
    - Fast Track 32%
    - Breakthrough 35%
    - Priority Review 57%
    - Accelerated Approval 16%
- Note: novel = active ingredient never approved before

Overpatented, Overpriced America's Bestselling Drugs of 2019 Source: https://www.i-mak.org/2019-bestselling/

Drug	Total patent applications	# Patents Issued	% Filed after FDA approval	Duration of patent protection	Patents filed in U.S. vs. Europe	Patents filed in U.S. vs. Japan
Xarelto	51	32	41%	33.5	1.5x	1.6x
Revlimid	196	109	74%	40.4	2.6x	2.6x
Opdivo	84	44	70%	35.1	2.2x	2.0x
Keytruda	129	86	50%	34.6	1.0x	1.2x
Imbruvica	165	88	55%	29.2	3.6x	3.9x
Humira	257	130	90%	39	3.3x	4.1x
Eylea	89	58	53%	39.7	3.2x	4.9x
Enbrel	68	39	76%	47.5	2.1x	2.6x
Eliquis	49	31	37%	33.8	2.7x	3.1x
Avastin	222	75	80%	41.6	2.4x	2.1x
Average	131	69.2	63%	37.5	2.5x	2.8x

Wall Street Punishes Low Rx Prices

- There are many more examples than these:
  - Gilead announces Remdesivir licensing agreements with low income countries – stock price drops 3%
  - Gilead announces a Remdesivir price of $5000 ($4500 was the cost-effective price analysis) – stock price increases 5%
  - Moderna issues highly tentative, non-scientific, early CV19 vaccine trial result in *press release*. Stock price soars 25%. Moderna execs sell their stock at market peak (and request more federal R&D funding).
- Stock grants are the largest part of C-suite executive compensation

Where we might be going

Market Disrupters

Medicare Negotiation – key points

- Focus on drugs in monopoly position – no competition.
  - Some drugs will be on patent via multiple patent applications
- Some exemptions from negotiation (not all)
  - Drugs with market competition
  - Drugs approved for only one indication/disease and that indication is a rare disease
  - A drug that is a small portion of total Medicare spend *and* the is the preponderant source of total company revenue (the small biotech exemption). Lasts only 3 years.
- Use existing net market prices as a key part of ceiling price
  - Drugs in monopoly position don't need to provide deep price concessions
  - Net and market price may look similar
- Negotiated price will be PUBLIC for other health plans and purchasers to see
  - It is included in Medicaid best price math – so Medicaid may get a benefit

Medicare Negotiations – possible short term effects

- Average launch price could grow fairly quickly because
  - MFP ceiling price is based on market prices
  - Medicare law and Medicaid law now have substantial rebate penalties for price increases in excess of CPI growth
  - Negotiation will involve comparing price to prices of therapeutic competitors
- Innovator life cycle management will change
  - Drug makers have spent decades on new ways to limit competition
  - Now manufacturers need to assure competition to be exempt from negotiation
  - Manufacturers have control of their patent rights and data exclusivities…
    - Manufacturers can share protected data with potential competitor
    - Result manufacturer maintains price and competitor launches at price higher than if innovator had an MFP and both are exempt from negotiation
    - Competition is good for consumers if PBM market behavior can be changed
- Will industry patent strategy change?
- Will the orphan drug designation gold rush slow down?

Other RX Market Disruptions – Pressure on Rx Price and Business Models

- These initiatives may also impact manufacturer market behavior
  - CIVICA Rx, CIVICA Script, Low Cost Drugs, state manufacturing
  - They all work with off-patent, non exclusivity products
  - Low Cost Drugs added patented Janssen product at reduced prices
  - CIVICA and Low Cost starting to work with employer health plans/insurance and creating new distribution channels to ensure supply chain commitment to low price.
- Brands bringing products to market with two list prices
- Employers creating new PBMs for greater control, flexibility to work with market disrupters, and better market behavior
- Brand insulin makers dropped their list price and created a dedicated distribution channel

More on Lilly Insulin Price Cuts

- Humalin insulin $66/vial from $275/vial for insured.
- Access at pharmacies contracted with Lilly and charge the low price.
- Insurers whose enrollees access Humalin must cap copay at $35/vial.
- Lilly will provide insulin to uninsured at $35/vial.
- Key points
  - Lilly and competitors may already be providing confidential rebates up to 70% off list price, so potential revenue loss is mitigated
  - Lilly creating a dedicated distribution channel
  - Requires a commitment from insurers/pbms in the program to set low copay

State Rx Rate Setting

- The time may be right to use statewide rate setting of certain high cost drugs to support disruption.
  - Make the price of the biosimilar the statewide upper payment limit to give the biosim a leg up against innovator attempts to quash biosim market access?
  - Potentially use rate setting to support stability in the multi-source generic market (other countries have done this)?
  - Take the money already on the table in the form of manufacturer rebates and price concessions and make the net of that an upper payment limit.
  - Focus on rx that have high patient cost sharing – that's a signal of an affordability problem, manage the cost and have insurers move the drug to a lesser cost share tier to improve access.
- Rate setting can drive down costs, get manufacturer discounts concessions to the consumer, expand access/improve sales, undermine anti-consumer business models

Prescription Drug Affordability Boards

- Prescription Drug Affordability Boards with Upper Payment Limits
  - CO, MN (awaiting Governor's signature), WA have full UPL authority. MD and OR have to return to legislature with a plan
  - ME, NH, NY have PDABs but these boards are not designed to lower costs statewide
  - PDAB bills introduced and debated in several additional states
    - VA billed passed Senate with R votes
    - NJ bipartisan support in Senate enough to pass a PDAB –negotiations with Governor who wants transparency
- Newest PDAB bills include Medicare Maximum Fair Price as statewide UPL
  - Extends Medicare's effort to all residents
- Statewide UPLs potentially the most effective policy
  - Affordability not value – value remains with providers, patients, and plans
  - Transparency through the supply chain to the patient at point of service
  - A statewide UPL has the potential to undermine all the current market shenanigans

Why Change is So Hard (besides the obvious)

- The whole market is a complex web of interactions and intersecting business models. Extremely difficult to understand all of it even for people in the market.
- Few good actors in this marketplace
  - Every participant has a profit motive, an angle, and a love of opacity.
  - Consumers are the only market participant without a business model or profit motive. Consumers take the brunt of the business model chess match.
- Need solutions that address all the misalignment -- such as statewide, all payor, all purchaser, rate setting for high cost drugs
- Hard to find expertise that isn't paid by pharma or otherwise profits more from high drug prices

Thank You!

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