Mission Possible

MOVING DIAGNOSTICS TO THE FOREFRONT OF PRECISION MEDICINE

by Hannah Mamuszka

An Unlikely Alliance – Could PBMs and diagnostic labs find synergies in the healthcare market?

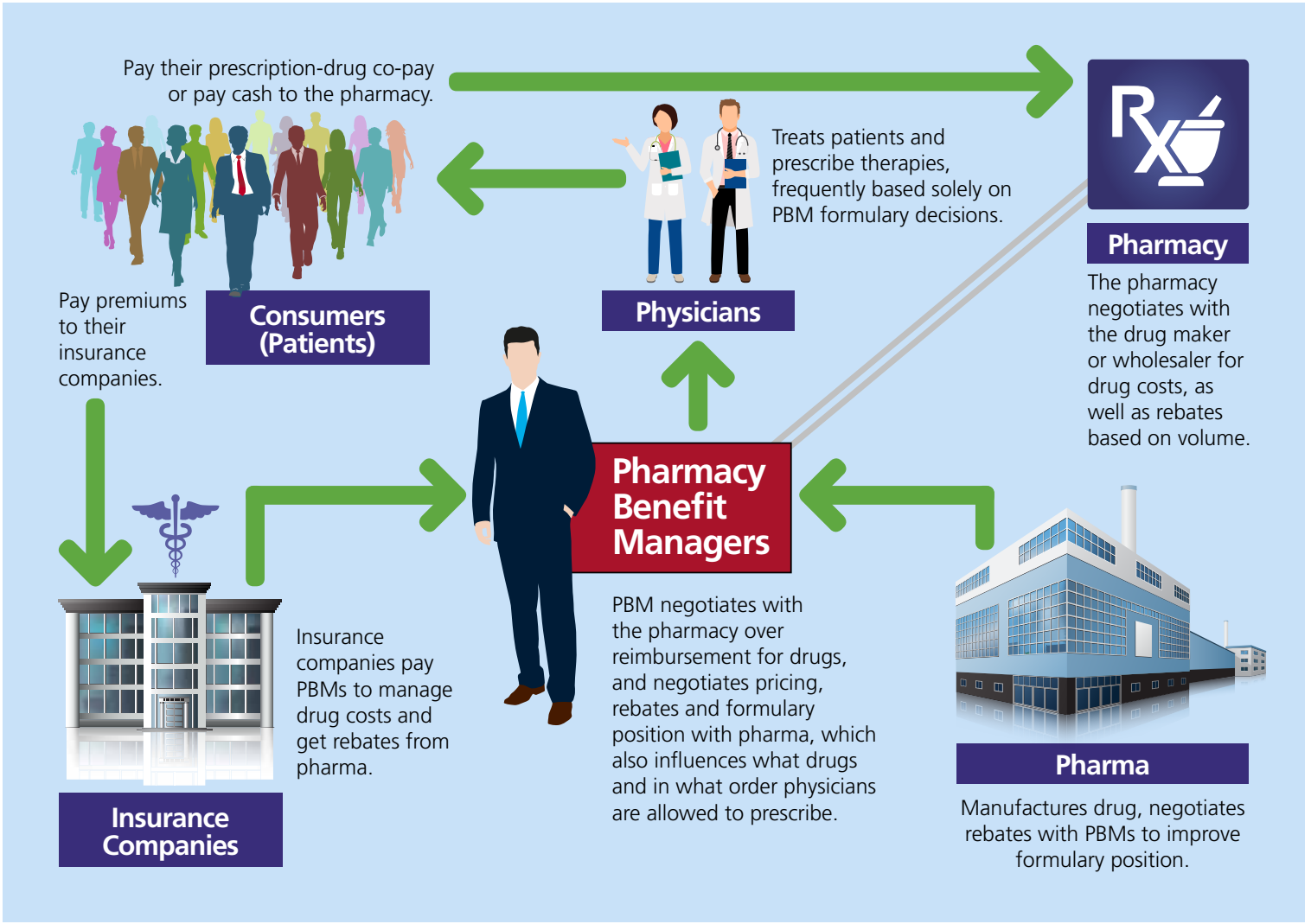
Pharmacy Benefit Managers (PBMs) have been all over the news in the past year, as the public has become more educated about their role in our healthcare system. They have been excoriated for lack of transparency in pricing, criticized for their role in inflating drug costs, and probably misunderstood a bit regarding the role they actually play. PBMs were created to address the fact that the US doesn't have a single-payer insurer that can negotiate with drug companies on price; their existence was meant to allow insurers and corporations to pool their resources through a cooperative group, which having the negotiating power of all of those parties together, should yield more leverage to payers and assert pressure on pharmaceutical companies and reduce drug spend. But in reality, this business has evolved to be something more financially substantial with more clinical authority than may have been intended.

Initially, PBMs were "middlemen" entities designated to process prescription medication claims (and paid a fee per claim) for insurance companies and large employer groups. However, in 2018, PBMs have leveraged their position and now impact almost every aspect of the prescription drug marketplace. In 2017, the top 3 PBMs (Express Scripts, Optum, and CVS) managed drug benefits for approximately 95% of the US population, representing 253 million American lives[1]. CVS may be more well known for the pharmacy storefronts, but 40% of their business comes their operations as a benefits manager[2].

The scope of business has expanded dramatically beyond just claims processing, into drug utilization review, drug plan formulary development, selection of which pharmacies are included in the prescription drug plan's network, determining how much network pharmacies will be reimbursed for their services, and operating mail order and specialty pharmacies themselves. In real terms, the PBM has as much say, if not more, in determining what drug a patient is prescribed as their physician does, and may make more money doing so than the pharmaceutical company who manufactured it.

PBMs negotiate with pharmaceutical companies on drugs and drug pricing across most diseases, to determine what level of rebates the company will offer for certain drugs, to incentivize (or disincentivize) their use. Rebates are paid directly to the PBM, and depending on the contractual relationship between the PBM and the health plan, some of the rebates may be passed on to either the health plan or the employer. Insurances companies and employers are the customers of the PBMs.

But none of those measures actually do anything about helping physicians choose effective therapies for their patients, because all of those decisions made by the PBM are based on marketing, pricing, and their ability to negotiate rebates on different tiers of pricing – not on whether one drug will work better for a group of patients than another. What happens in disease indications where multiple drugs are approved – how do ›



physicians make a decision on what drug to prescribe for their patients? Frequently, they don't choose – the PBM has chosen for them. In the absence of other tools, PBMs dictate the formulary of drugs – meaning what drugs can be used for what diseases, in what order.

What if there were diagnostic tools available, to stratify patients for response/non-response to drugs? What if that information was used to determine in what order patient received therapy? How would that change cost structure, patient management, and outcomes?

This is not to say that PBMs and diagnostics can't work together – quite the contrary. The value of PBMs was foremost in moving volume from brand name drugs to generics.

This shift is largely complete – a record 87% of prescriptions were dispensed as brand name generics in 2017[1]. PBMs must now continue to prove their value in the specialty drug sector, which involves a degree of sophistication and innovation. Specialty drug dispensing requires an increased focus on evidence-based protocols, and adherence models. Unfortunately, PBMs are being forced to innovate in a time when their customers don't trust them very much. The statistics are sobering – 7/10 employers would 'welcome an alternative to a rebate-driven approach to managing costs', while only 41% of employers rate PBMs as 'very good' in their core competency – rebate negotiations[2]. Put another way, PBMs are being forced to differentiate themselves in specialty pharmacy, where their core competency is not sufficient to solve the problem for their customers. But diagnostics could be their 'alternative' secret weapon.

"We see molecular diagnostics being a significant opportunity for the PBMs", said Matthew Rosamond, a director in PricewaterhouseCoopers' health industries practice in 2010. It seems that Mr. Rosamond's prediction is beginning to come to fruition. PBMs are actively scouting for diagnostics that can make some – sometimes any – dent in the tide of rising specialty drug costs. Kroger Prescription Plans recently made headlines with its forward-thinking offering of Vectra DA as a benefit option for employer

group clients. "The cost of care for patients with rheumatoid arthritis has skyrocketed and specialty drugs to treat autoimmune diseases now comprise approximately ten percent of pharmacy spending in the United States," said Rich Adams, senior vice president at Kroger Prescription Plans. Just think – if PBMs are embracing Vectra DA, a disease activity test that does not direct therapeutic decisions as linearly as response-non-response diagnostics can, how much more should PBMs be embracing diagnostic testing that does have these capabilities?

Let's consider a couple of examples. Take rheumatoid arthritis, where patients with advancing disease have multiple options including:

Anti-TNFα inhibitors {Adalimumab (Humira), Etanercept (Enbrel), Infliximab (Remicade) Certolizumab (Cimzia) Golimumab (Simponi)}
JAK inhibitors (Tofacitinib) (Xeljanz)
CD80 inhibitors (Abatacept (Orencia)
IL-1Ra (Anakinra (Kineret)
CD20 (Rituximab (Rituxan)
IL-6 (Tocilizumab (Actemra)

- Completely different mechanisms of action
- Response rates between 20-35%; FDA and clinical consortia do not recommend use first
- All have significant side effect profiles
- No diagnostic tests currently available to determine likelihood of response vs non-response

What is the result? ~90% of patients are put in anti-TNF therapies as first line therapy, not because they are the most effective therapies or have the lowest rates of adverse events or are the least expensive therapies, but simply because of rebates back to PBMs.

What about Multiple Sclerosis? In relapsing-remitting MS, the most common form, there are many FDA approved options for treatment:

- Beta interferons
- Ocrelizumab (Ocrevus)
- Glatiramer acetate (Copaxone)
- Dimethyl fumurate (Tecfidera)
- Fingolimod (Gilenya)
- Teriflunomide (Aubagio)
- Natalizumab (Tysabri)
- Alemtuzumab (Lemtrada)

All of these drugs are approved for the treatment of relapsing-remitting multiple sclerosis. There are no biomarkers for any of these drugs, to indicate if a patient is likely to respond or not respond, despite the fact that the mechanisms by which the drugs work are completely different. The side effect profiles are completely different. So… how does a physician make their choice?

The answer? Too frequently, they don't get to. The choice is made for them, based on the formulary, negotiated by the PBM. PBMs argue that they are most effective in disease areas where there are multiple drugs approved with a similar level of evidence, because that is where the negotiating power of the combined network should bring the largest rebates and the lowest prices. The National Multiple Sclerosis website suggests that when changing health plans, patients check out formulary tiers to make sure that if they are on a drug that is working on for them that it is on the formulary in a spot that allows you to access it. Otherwise, if you switch health plans, you may have to switch medications. Not for a medical reason- but because the PBM negotiated a different discount for a different drug on a different plan.

One of the primary measures that PBMs have implemented is called 'Step Therapy', whereby patients are required to start on the least expensive medications first before they can progress to more expensive medications. Looked at from a strictly financial perspective, with no other tools to determine if a patient will respond to any of the drugs, this makes sense, but from a clinical perspective, can be problematic. In progressive diseases, such as rheumatoid arthritis, multiple sclerosis, Crohn's disease, psoriasis, and many others, step therapy requires the patient to start on and prove failure of response to a therapy, before the patient is allowed to try another therapy. While the patient is progressing through the therapy 'steps', the disease continues to progress and symptoms worsen, often irreversibly. Proving step therapy can take years before a patient finds a therapy that works for them.

Now imagine a world where diagnostic tools for stratifying patients for all of these therapies was available. Every drug developed over the past 20 years is a rationally designed targeted therapy, and now diagnostic technology has caught up to drug development and each drug could have a diagnostic classifying tool. If we had the diagnostic tools to determine which patients would respond to each class of therapy, and which patients were most at risk for adverse events from a class of drugs, we could both steer patients towards effective therapies and steer them away from ones likely to be dangerous for them, based on the biology. Instead of requiring patients to go on 'step therapy', where they are forced to try the cheapest drugs on formulary first, we could have patients assigned to the therapy most likely to be effective first, giving patients the best chance for meaningful outcomes from the start based on scientific and clinical data, not just the hope that the cheapest drug will work. ■

Hannah Mamuszka is Founder and CEO at Alva 10. Alva 10 is focused on moving diagnostics to the forefront of Precision Medicine by executing a comprehensive strategy of value, economics, technology in diagnostic development and commercialization. www.alva10.com

References

1. https://accessiblemeds.org/sites/default/files/2018-02/Doug%20Long.pdf
2. https://www.drugchannels.net/2017/11/if-employers-are-so-unhappy-with-their.html