

Precision Medicine: The Role of Pharmacists and Reimbursement Challenges

“Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals. You can match a blood transfusion to a blood type — that was an important discovery. What if matching a cancer cure to our genetic code was just as easy, just as standard? What if figuring out the right dose of medicine was as simple as taking our temperature?”¹

Introduction

With these words in 2015, President Barack Obama announced a \$215 million commitment to research and development of treatment and prevention strategies tailored to a patient’s unique characteristics, including his or her genome sequence. This Precision Medicine Initiative put impetus behind the concept of personalized medications, foreseen as powerful tools for achieving drug efficacy while avoiding adverse drug events and reducing healthcare costs through prevention of drug-related hospitalizations.

While the promise of precision medicine is monumental, delivery is not without stumbling blocks and a great deal of change and effort will be required by all stakeholders. In this paper, we focus on one key participant – the pharmacist – with emphasis on some of the challenges in the reimbursement process.



Today, medication response rates can be as low as 25 percent for some medication classes. At the same time, adverse drug reactions are the fourth leading cause of death and an important cause of hospitalization.²

What is Precision Medicine?

Precision Medicine is a treatment option tailored to groups of patients based on laboratory results that show predictive biomarkers (which indicate who is likely to benefit from the drug) or to individuals based on their unique genetic profile or status, such as age and gender.³

At the core of Precision Medicine is Pharmacogenomics (PGx), the study of how genes affect a person’s response to drugs. This relatively new field combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop effective, safe medications and doses that will be tailored to a person’s genetic makeup.⁴

This emphasis on biomarkers – measurable substances in the body whose presence is indicative of phenomena such as disease, infection or environmental exposure – is a far different approach to the traditional “one-size-fits-all” model of designing drugs for the “average” patient.⁵ Tested on broad populations and prescribed using statistical averages, these conventional pharmaceuticals work for some patients but not others, due to genetic differences. This has led to a situation in which any given prescription drug now on the market works for only about half the patients who take it, according to Jackson Laboratory, an independent, nonprofit biomedical research institution.⁶

Precision medicine, on the other hand, incorporates patient-specific information and biomarkers to help inform decisions as to optimal treatment for complex disease states. With this approach, physicians and pharmacists also can identify patients susceptible to adverse effects; be aware of dangerous drug-drug, drug-gene and drug-drug-gene interactions; and provide care in a whole new way that is completely individualized.⁷

Drug-drug interactions, of course, are widely recognized, but the other two newly described interactions may be less so. In that regard, a drug-gene interaction occurs when a patient's genetic CYP450 type (e.g., CYP2D6 poor metabolizer) affects that patient's ability to clear a drug. A drug-drug-gene interaction occurs when the patient's CYP450 genotype and another drug in the patient's regimen (e.g., a CYP2D6 inhibitor) affect that individual's ability to clear a drug.⁸



A recent study found that one-time pharmacogenomic testing is cost-effective for preventing adverse drug reactions over a patient's lifetime.⁹

Precision medicine also is seen as a significant tool in reducing emergency hospitalizations or avoidable readmissions. A case in point: Of the five medications that most often cause emergency hospitalization due to adverse drug events, science has shown that genetic implications in an individual's metabolism influence the safety and efficacy of four.¹⁰

Incorporating this key biological data with the social and behavioral aspects of a patient is anticipated to play a major role in proactive and preventative care, further improving health and reducing costs. In addition, laboratory testing can play a role in drug development by helping identify potential candidates for clinical trials.

The Role of Pharmacists

As noted by Ed Abrahams, CEO of the Personalized Medicine Coalition (PMC) advocacy and education group, this new era has "enormous ramifications" for pharmacists. "[They] are on the front line of the actual prescribing," he said, "and [this] will have to be individualized, based upon certain diagnostic tests in the future."¹¹

Experts agree that it will take concerted effort by pharmacists to leverage their "front-line" expertise to take their rightful place as important constituents and leaders in the move to precision medicines. This will require the acquisition of new knowledge and even greater emphasis on their long-standing role as trusted advisors.

Keeping Up With Advancements

Precision medicines are currently on the market, with many focusing on cancer treatment.¹² As the past five years have seen a surge in new precision medicines — and spending on them — and there are more in the pipeline, exponential growth is expected. Thus it is important for pharmacists to be aware of these medications and thoroughly understand them and their implications. This will require decision-support tools able to provide new and changing drug information to clinicians quickly.

Staying Current on Availability

Given the expected surge, some experts have expressed doubts as to whether the current healthcare system is advancing fast enough to ensure patients will benefit from personalized medications. Precision medicines have unique traits that the current health care framework does not adequately support.¹³ As noted, decision-support tools and instantly accessible databases already are available to pharmacists, potentially positioning them for a leadership position in the transition to precision medicine.

Personalized medicines accounted for nearly one of every four FDA approvals from 2014 to 2016, and the PMC estimates that more than 70 percent of cancer drugs now in development are personalized medicines.

Educating and Advocating

Pharmacists also may need to use their specific expertise to educate clinicians, explaining the benefits of a recommended PGx to providers with less understanding of them. This can assure patients get the right tests and, subsequently, the right medication, while expanding the provider knowledge base.

Coordinating Care

Precision medicine may well usher in a new level of collaboration between pharmacists and medical providers, with the former relying on the latter’s authorization and providers depending upon the pharmacist’s clinical guidance in interpreting and applying the resulting test data.¹⁶ Key elements of patient interpretation will include:

- Using all available information to recommend the optimal drug and dosage regimen.
- Considering drug-drug-gene interactions and alerting the physician when a medication is not suitable for a patient.
- Relaying, based on genome information, facts such as a patient’s lacking a certain enzyme used to metabolize a drug or having extra drug-metabolizing enzymes.
- Noting, when data indicates, that a patient is likely to contract cancer or heart disease for integration into decision making.
- Making recommendations to help alleviate adverse drug reactions and promote improved therapeutic outcomes.
- Documenting all results.

Advising Patients

As medical testing results grow more detailed and complicated, affected patients likely will need additional counseling to help them understand why a drug was chosen, assure its proper use and quell any concerns they may have about use of genetic information. In this area, pharmacists already are trusted as knowledgeable and reliable medication resources and, often, have established relationships with patients. They also will play a key role in monitoring of patients and their response to prescribed therapy.

An Important First

On May 23, 2017, the U.S. Food and Drug Administration granted accelerated approval for Keytruda, a drug designed to help the immune system recognize and destroy cancer cells by targeting a specific cellular pathway. This action marked the first time the agency has approved a cancer treatment based on a common biomarker rather than the location in the body where the tumor originated.¹⁴

In an opinion piece on STAT, PMC CEO Abrahams called the approval an “important first for the field of personalized medicine, which anticipates an era in which physicians use molecular tests to classify different forms of cancer based on the biomarkers they express, then choose the right treatment for it.”¹⁵

He contrasted this with traditional cancer treatments, which are distributed to large populations even though only a fraction of those patients will benefit. Keytruda, on the other hand, was approved only for the 4 percent of cancer patients whose tumors exhibit the biomarker. The latter, he added, may help the health system save money by focusing resources only on patients who are likely to benefit from Keytruda.

Since 45 percent of these [precision] medicines are coming to market with “black box warnings” indicating evidence of an association with serious hazard, pharmacist engagement with patients is . . . important. Pharmacists can enroll patients in pharmacovigilance programs. And when serious side effects are possible, the relationship that patients have with the pharmacist can help those side effects be more quickly identified. It’s critical for pharmacists to step up and play the fullest role they can.”¹⁷

As there will be times when the pharmacist receives pharmacogenomic results for a patient that indicate a medication will not work in his or her body or a biomarker that shows the person has an increased risk for another disease state, many situations require a great deal of finesse and, some, referral to a genetic counselor. It is important for pharmacists to remember that some results, such as a gene linked to Alzheimer’s, could be devastating to patients, while other conclusions may motivate patients to make lifestyle changes to counter their genetic disposition to a condition such as coronary artery disease.¹⁸ This catapults the pharmacist into a new realm of responsibility and requires a high level of knowledge – of science and the patient.

For instance, according to Sandra Leal, vice president at SinfoniaRx, pharmacogenomic test results often come back with multiple findings, which the pharmacist can stratify to determine which to react to first based on adverse effects, adherence issues or clinical instability that the patient might be experiencing. Appropriate use of test results, she added, requires a thorough review of medications the patient is using, including OTCs and herbal supplements. The pharmacist, she said, “plays a critical role in medication reconciliation and in obtaining a history of lifestyle issues that might contribute to the findings . . . If the history and the medications are not completely obtained, this may impact the findings.”¹⁹

Putting It All Together

There is no doubt that the role of the CNE is both critical and complex. However, with the right tools in place, he or she can contribute even more to a facility’s informational and educational needs. With immediate access to authoritative sources and up-to-date content through technology that is built strictly for healthcare, today’s Clinical Nurse Educators can use their time more effectively and work more efficiently for enhanced job performance and satisfaction.



More than 250 prescription medication labels now include information from the FDA for people with certain genetic variations.²⁰

Overcoming Reimbursement Challenges

Despite the amazing potential of precision medicine, reimbursement remains its No. 1 barrier, as validated unanimously at the International Molecular Diagnostics Congress in Barcelona in 2016. Always a complicated process, health insurance coverage and reimbursement will become even more complex with this new emphasis on genetic testing, requiring engagement by payers and significant changes in their policies.

An example is found in the approval of Keytruda, the first tissue- and site-agnostic cancer treatment (see sidebar). Traditionally, payer policies have been driven by specific cancer type approvals, based on efficacy shown in clinical trials. Drugs such as Keytruda, experts note, will require payers to open their authorization criteria to address this open-ended indication based on genomic profiling.²¹ Similar, and equal, challenges abound.

For pharmacy, other issues include reimbursement for the pharmacist's time in providing the consultation and for the pharmacogenomic test itself, which remains cash-based as it is not billable as a Medication Therapy Management service.

One initiative under way involves establishing new American Medical Association Molecular Pathology CPT codes for pharmacogenomic testing – making sure all Clinical Pharmacogenomics Implementation Consortium guidelines have a CPT code for the associated gene and moving those from tier 2 to tier 1 to assure payment by Medicare contractors and insurers. Success, one participant reported, will drive insurers either to price the tests or determine there is no coverage.

On their part, PBMs, which have a particularly far reach and much to gain in avoidance of side effects, are building lab networks with contracted terms to reduce costs for payers.

Going forward, experts say, the solution to this highly complex issue will require the creation of proper incentives and business models from payers that reflect the steps, effort [and value] of the process of identifying patients' profiles and optimal treatment. First, however, Abrahams has said, it is critical that payers fully understand that precision medicine's role in increasing efficacy and getting it right the first time not only improves patient outcomes but decreases systemic costs.²²

Conclusion

Despite its myriad and concomitant challenges, the concept of precision medicine will only get more exciting as science and technology continue to advance. As experts in medications and their effects on the body, it has been noted, pharmacists are poised to become the point persons for the safe and ethical use of this tool,²³ playing a significant role in the next era of healthcare delivery. Their ability to participate fully in precision medicine, however, will be dependent on the successful integration of all stakeholders and industry-wide development of new processes.

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- ¹White House, Precision Medicine Initiative, January 2015, <https://obamawhitehouse.archives.gov/node/333101>
- ²Donald W. Light, New Prescription Drugs: A Major Health Risk with Few Offsetting Advantages, Harvard University, Edward J. Safra Center for Ethics, June 27, 2014, <https://ethics.harvard.edu/blog/new-prescription-drugs-major-health-risk-few-offsetting-advantages>
- ³Drug Store News, Quintiles IMS report discusses pharmacists' roles regarding precision medicines, May 23, 2017, <http://www.drugstorenews.com/article/quintilesims-report-discusses-pharmacists-roles-regarding-precision-medicines>
- ⁴National Institutes of Health, Genetics Home Reference, What is pharmacogenomics?, October 17, 2017, <https://ghr.nlm.nih.gov/primer/genomicresearch/pharmacogenomics>
- ⁵White House, Precision Medicine Initiative, January 2015, <https://obamawhitehouse.archives.gov/node/333101>
- ⁶The Jackson Laboratory, What Is Precision Medicine?, <https://www.jax.org/research-in-action/precision-medicine-and-you/what-is-precision-medicine>
- ⁷Rebecca Tomich, Pharm.D, Joe Brown, B.S. Pharm, The Pharmacist's Role in Personalized Medicine: A Review of Pharmacogenomics, Michigan Pharmacists Association, <http://www.michiganpharmacists.org/Portals/0/education/cearticles/pharmacogenomics012016.pdf>
- ⁸Verbeurgt P1, Mamiya T, Oesterheld J, How common are drug and gene interactions? Prevalence in a sample of 1143 patients with CYP2C9, CYP2C19 and CYP2D6 genotyping. *Pharmacogenomics*. 2014 Apr;15(5):655-65. doi: 10.2217/pgs.14.6.
- ⁹American Pharmacists Association, Pharmacists' role in pharmacogenomics increasing in an age of precision medicine, *Pharmacy Today*, July 2016, Volume 22, Issue 7, Pages 40–43, [http://pharmacytoday.org/article/S1042-0991\(16\)30528-X/fulltext](http://pharmacytoday.org/article/S1042-0991(16)30528-X/fulltext)
- ¹⁰Pharmacy Times, The Role of the Pharmacist in Pharmacogenomics, August 24, 2016, <http://www.pharmacytimes.com/publications/issue/2016/august2016/the-role-of-the-pharmacist-in-pharmacogenomics>
- ¹¹Quintiles IMS Institute, Global Oncology Trends 2017, http://www.imshealth.com/en/thought-leadership/quintilesims-institute/reports/global_oncology_trends_2017
- ¹²Drug Store News, QuintilesIMS report discusses pharmacists' roles regarding precision medicines, May 23, 2017, <http://www.drugstorenews.com/article/quintilesims-report-discusses-pharmacists-roles-regarding-precision-medicines>
- ¹³Ibid.
- ¹⁴FDA News Release, FDA approves first cancer treatment for any solid tumor with a specific genetic feature, May 23, 2017, <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm560167.htm>
- ¹⁵STAT, Landmark FDA approval bolsters personalized medicine, JUNE 21, 2017, <https://www.statnews.com/2017/06/21/personalized-medicine-cancer-keytruda-fda/>
- ¹⁶American Pharmacists Association, Pharmacists' role in pharmacogenomics increasing in an age of precision medicine, *Pharmacy Today*, July 2016, Volume 22, Issue 7, Pages 40–43, [http://pharmacytoday.org/article/S1042-0991\(16\)30528-X/fulltext](http://pharmacytoday.org/article/S1042-0991(16)30528-X/fulltext)
- ¹⁷Drug Store News, QuintilesIMS report discusses pharmacists' roles regarding precision medicines, May 23, 2017, <http://www.drugstorenews.com/article/quintilesims-report-discusses-pharmacists-roles-regarding-precision-medicines>
- ¹⁸Rebecca Tomich, Pharm.D, Joe Brown, B.S. Pharm, The Pharmacist's Role in Personalized Medicine: A Review of Pharmacogenomics, Michigan Pharmacists Association, http://www.michiganpharmacists.org/Portals/0/education/cearticles/pharmacogenomics_012016.pdf
- ¹⁹American Pharmacists Association, Pharmacists' role in pharmacogenomics increasing in an age of precision medicine, *Pharmacy Today*, July 2016, Volume 22, Issue 7, Pages 40–43, [http://pharmacytoday.org/article/S1042-0991\(16\)30528-X/fulltext](http://pharmacytoday.org/article/S1042-0991(16)30528-X/fulltext)
- ²⁰U. S. Food & Drug Administration, Table of Pharmacogenomic Biomarkers in Drug Labeling, October 3, 2017, <https://www.fda.gov/Drugs/ScienceResearch/ucm572698.htm>
- ²¹Health Business Daily, First Tissue-Agnostic Cancer Drug Could Pose Challenges for Payers, June 27, 2017 https://aishealth.com/archive/nsprn0617-04?utm_source=Real%20Magnet&utm_medium=email&utm_campaign=114387239
- ²²Modern Medicine Network, Drug Topics, Personalized medicine and the future of pharmacy, June 15, 2010, <http://drugtopics.modernmedicine.com/%5Bnode-source-domain-raw%5D/news/modernmedicine/modern-medicine-feature-articles/personalized-medicine-?page=full>
- ²³American Pharmacists Association, Pharmacists' role in pharmacogenomics increasing in an age of precision medicine, *Pharmacy Today*, July 2016, Volume 22, Issue 7, Pages 40–43, [http://pharmacytoday.org/article/S1042-0991\(16\)30528-X/fulltext](http://pharmacytoday.org/article/S1042-0991(16)30528-X/fulltext)