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Medication MANAGEMENT

SUPPORTING PLAN MEMBER HEALTH

ABOUT

Medication Management is an educational series that takes a closer look at maximizing plan sponsors' investment in drug plans, which includes supporting plan members to be healthy while continuing to protect plan sponsors' bottom lines.

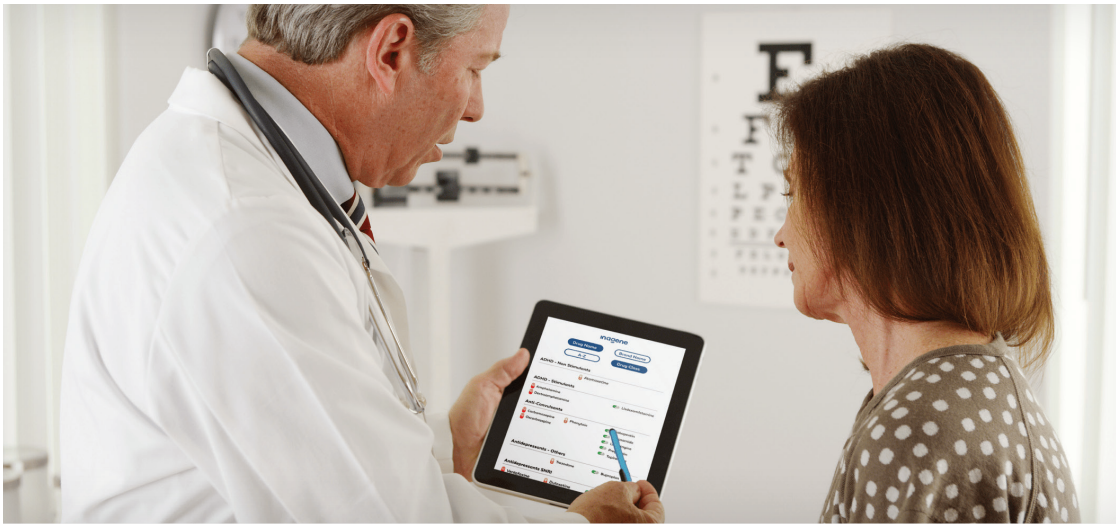
As the Canadian health-care system evolves, there are a wide variety of tools, technology and programs that can support patients and improve health outcomes, in addition to ensuring long-term benefit plan sustainability.

This installment of *Medication Management* provides readers with practical guidance on what to look for when selecting a pharmacogenetic testing provider.

WHAT IS PHARMACOGENETIC TESTING?

Pharmacogenetic testing (PGx) considers a patient's genetic makeup to assess their response to different medications and provides personalized recommendations on optimal dosages. It can help determine which medications would be safest, most effective and have the highest likelihood of clinical response for an individual patient.

PGx has the potential to lower group benefits costs, particularly with respect to mental health and pain, by preventing drug wastage and reducing disability and absenteeism.



Pharmacogenetic testing in Canada – what plan sponsors need to know

Important Considerations when Navigating the Canadian Landscape

Pharmacogenetic testing is quickly becoming a core part of Canadian employee benefits packages; however, there is significant variability between providers and tests. "No two tests are the same," says Chad Bousman, MPH, PhD, associate professor, department of medical genetics, University of Calgary. Bousman also heads the psychiatric pharmacogenomics (PsychPGx) lab that works to discover, develop and evaluate genomic-based tools with the utility to guide clinical decision-making and improve mental health outcomes.

The greatest differences between tests, Bousman says, "are typically a matter of which genes and alleles are tested, but they often also differ in how they translate the genetic results into clinical recommendations."

According to John Papastergiou, community pharmacist and assistant professor at University of Toronto, "due diligence is important because not all tests are created equal."

The lack of Canadian regulation and standardization of pharmacogenetic testing can lead to questionable and potentially unsafe outcomes for plan members, which is why it's important for plan sponsors to assess their pharmacogenetic testing provider.

> "Due diligence is important because not all tests are created equal."
>
> –John Papastergiou

This guide will assist plan sponsors in ensuring they choose, or have already selected, credible, evidence-based pharmacogenetic testing partners and/or in deciding which tests to reimburse.

Pharmacogenetics 101

Pharmacogenomics studies how genes affect a person's response to drugs, whereas **pharmacogenetic** testing looks at an individual's specific genes to predict how they might respond to different medications to determine the most appropriate treatment and dosage for them. Pharmacogenetic tests are different from general **genetic tests**, which are used to diagnose or identify risks for disease.

What factors should be considered when assessing a pharmacogenetic test provider?

Plan sponsors looking to ensure desired outcomes are achieved with PGx testing should carefully vet their providers.

Plan sponsors should ensure tests are:

☑ 1. As comprehensive as possible in the therapeutic areas that most commonly drive disability

a. **Include pharmacokinetic and pharmacodynamic variants.**

Pharmacokinetic gene variants impact how the drug is metabolized or broken down or eliminated by the body.

Pharmacodynamic gene variants impact how well the body will respond to the drug.

b. **Include as many of the specific genetic variants as possible that are known to specifically impact metabolism of drugs to treat mental health and pain, which are some of the biggest disability drivers.** It is not enough to simply test for a specific gene, because each gene can have multiple variants that impact drug response in different ways. "I look for how many genes they are evaluating that are specific to pain and psychiatric conditions," says Karen Adams, president CloudMD, "because the more comprehensive the panel, the more likely we will get the information we need."

c. **Include only drugs with recognized gene drug links that are specifically available in Canada.** The inclusion of drugs that are not available in Canada provides no useful purpose for appropriate prescribing for Canadians.

> "Unfortunately, many laboratories test for genes that do not have pharmacogenetic-based dosing guidelines developed by expert groups, which may result in questionable clinical validity."
>
> –Chad Bousman

d. **Include only drugs with recognized gene drug links and guidelines developed by expert groups.** Including drugs that have no gene-drug links and simply always marking them as "use as directed," adds no value. "Unfortunately," explains Bousman, "many laboratories test for genes that do not have pharmacogenetic-based dosing guidelines developed by expert groups, which may result in questionable clinical validity."

Where do PGx recommendations come from in evidence-based tests?

There are several international consortiums commissioned by the FDA and other regulatory bodies that translate pharmacogenetic research and evidence into clinical practice via guidelines and recommendations.

These are the Clinical Pharmacogenetics Implementation Consortium (CPIC), the Pharmacogenomics Knowledge Base (PharmGKB) and the Dutch Pharmacogenetics Working Group (DPWG).

They conduct a critical appraisal of the evidence, grade it and ultimately develop recommendations for gene-drug pairs to support clinical decision-making, which are regularly updated.

These guidelines should be used by PGx providers to produce evidence-based tests and recommendations.

e. **Include rare variants.** Many clinically significant genetic variants occur very rarely and may impact how people of different races and ethnicities respond to medications. Tests that include only variants that occur most frequently in a population may provide an incomplete picture and ultimately incorrect or incomplete recommendations. "Consider a service provider that looks at the highest number of genes and the highest number of variants," says Papastergiou, because it predicts drug metabolism for a broader population group. "This is important where we work in Toronto because we have so many multiethnic patients."

f. **Include as many drugs as possible with recognized gene-drug links for some of the biggest disability drivers: mental health and chronic pain.** This increases the likelihood that plan members at risk of disability due to these conditions will receive valuable insights from testing. This may include both prescription and over-the-counter medications, as well as cannabis.

Why include cannabis?

Cannabis is becoming a mainstream treatment for mental health and pain. There can be significant individual variations in treatment response, dosing requirements and optimal CBD:THC ratio, in addition to unexpected, gene-driven side effects or drug-drug interactions.

Potential impact

> "A poor-quality test has the potential to unfavourably tilt the risk-to-benefit ratio."
>
> –Chad Bousman

"A poor-quality test has the potential to unfavourably tilt the risk-to-benefit ratio," explains Bousman. Questionable clinical validity of test results could result in negative health outcomes if a potentially efficacious drug is denied, or a recommended drug is not suitable for the patient or goes against clinical guidelines.

☑ 2. Accessible and simple to use

a. **Available direct to the plan member** or from their pharmacist without necessitating a physician request. While many may hesitate to order a genetic test if recommended by their employer/insurer, they may get tested if it is on the recommendation of their trusted pharmacist. The member's pharmacist may also be best qualified to determine if they could benefit from testing, and could provide a consult on the results. This increases the chance that the member in need will be tested and avoids delays in getting physician approval, both of which could make the difference in avoiding disability.

> "Once someone decides to take a PGx test, waiting for the results can make them very anxious. Some providers take seven days, while others can take up to 30 days, which can be too long."
>
> –Karen Adams

b. **Results delivered quickly** (ideally within five to seven days) ensures timely access to the most appropriate treatment. Reducing wait time by two to four weeks could make the difference in preventing a plan member from having to go on disability. Timing to receive results can vary significantly between providers, says Adams: "Once someone decides to take a PGx test, waiting for the results can make them very anxious. Some providers take seven days, while others can take up to 30 days, which can be too long."

c. **Affordable**, which makes them accessible to more patients and provides a better return on investment.

d. **Simple and easy to interpret reports** ensure the plan member's own healthcare team can quickly act on the results without necessitating the additional intervention of the PGx company's pharmacist to first interpret and translate them, driving further delays. Of importance, this also ensures prescribers can continue to leverage the test results over the months and years that follow as the member's treatment plan changes, driving ongoing return on test investment.

e. **Easy and secure sharing of report between patient and their healthcare team** will maximize chances that test results will be applied to treatment. Some companies' reporting platforms are better than others, says Papastergiou. "If [the]data reported and [the] platform meet the needs of clinicians, it results in a quicker and better intervention." Adams wants "a report that allows collaboration between the patient, their family doctor, specialist, pharmacist and nurse navigator."

f. **Report includes direct links to all data sources**, which provides transparent and easy access to recommendations, evidence and additional contextual information.

☑ 3. Supported by appropriate evidence, vigilance and quality control

Because pharmacogenetic testing is not tightly regulated in Canada, providers can make claims and not be held accountable for the accuracy and specificity of the tests they provide, which could potentially lead to negative health outcomes.

Tests should:

a. **Be developed and maintained by appropriately qualified genetic experts.** Plan sponsors should be sure that the test was developed and is regularly updated by experienced and qualified geneticists who are considered experts in the field of genomics and pharmacogenomics.

> "We want to ensure that the recommendations are based on existing guidelines."
>
> –John Papastergiou

b. **Be transparent and credible in how test results are translated into recommendations.** "We want to ensure that the recommendations are based on existing guidelines," says Papastergiou. Some providers use proprietary algorithms to interpret the results, which makes it difficult to assess the evidence that supports their recommendations. Bousman recommends that "the testing laboratory be transparent about which genes and alleles are tested and how the results are translated into prescribing recommendations."

c. **Be approved by an independent accrediting body** (see Regulation and Accreditation).

d. **Be regularly updated at no cost**, to include the most recent science and evidence as it evolves. The science of PGx is evolving rapidly, with new drugs and recommendations added each year. With regular updates, investment in the tests provide increasing returns over time and ensure recommendations are always based on the latest findings.

e. **Be conducted in Canada.**

Provider should:

a. **Be an accredited laboratory certified as a pharmacogenetic testing provider**, which is essential to ensuring accuracy and reliability of pharmacogenetic test results. "Providers that have their certification from Clinical Laboratory Improvement Amendments (CLIA) and a Health Canada Medical Device Establishment Licence (MDEL) gives me confidence on quality and the backing," says Adams (see Regulation and Accreditation).

b. **Not be outsourcing testing to a third-party lab**, which can slow the process and impact oversight and quality control.

c. **Be fully compliant with the Personal Information Protection and Electronic Documents Act (PIPEDA) and all national and provincial privacy laws.**

d. **Be actively engaged in ongoing research** to further the science and support ongoing updates.

REGULATION AND ACCREDITATION

"Pharmacogenetic testing in Canada is largely unregulated and unstandardized. There is no regulation or standardization on which genes are tested from laboratory to laboratory."

–Chad Bousman

According to Bousman, "Pharmacogenetic testing in Canada is largely unregulated and unstandardized. There is no regulation or standardization on which genes are tested from laboratory to laboratory, despite the availability of pharmacogenetic-based dosing guidelines for 23 genes and 82 drugs developed by expert groups around the globe."

Regulation

The United States more tightly regulates pharmacogenetic testing, in contrast to Canada. In the US, the Clinical Laboratory Improvement Amendments (CLIA) regulate laboratory testing and issue multiple types of CLIA certificates based on the kinds of diagnostic tests a lab conducts, including certification of labs specifically offering PGx tests. The FDA recently expressed concerns about some pharmacogenetic tests that make claims that may not be supported by scientific and clinical evidence, and therefore may not be accurate, leading to potentially serious health consequences for patients.[1]

Canadian Medical Association

Like the US FDA, the Canadian Medical Association has called for greater regulatory guidance and protection of testing in Canada to ensure that individuals are not adversely affected by results that are not predictive or accurate.[2] It recommends that physicians make use of clinically valid tests and accredited laboratories, and that scientific evidence describing the validity and utility of a test should be clearly stated in language that is easy to understand.[3]

The Clinical Laboratory Improvement Amendments

The US Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulations ensure quality laboratory testing by regulating and certifying American facilities that test human specimens for health assessment or to diagnose, prevent or treat disease.[4] CLIA accreditation is also available to Canadian PGx providers that are able to meet the CLIA's stringent certification requirements.

Health Canada's Medical Device Establishment Licence

A Medical Device Establishment Licence (MDEL) provides Health Canada assurance that the facility meets safety requirements to protect the public should a problem be identified.[5]

1. https://www.fda.gov/news-events/press-announcements/jeffrey-shuren-md-jd-director-fdas-center-devices-and-radiological-health-and-janet-woodcock-md

2. https://policybase.cma.ca/documents/Policypdf/PD17-05S.pdf

3. https://www.cma.ca/sites/default/files/2018-11/cma-policy-direct-to-consumer-genetic-testing-pd17-05-e.pdf

4. https://www.cdc.gov/clia/about.html

5. https://health-products.canada.ca/mdel-leim/index-eng.jsp