CPIC Oct 3, 2019

Proposed Local Coverage Determination (LCD): MolDX: Pharmacogenomics Testing (DL38294)

This is a limited coverage policy for CYP2D6, CYP2C19, CYP2C9, HLA-B*15:02, HLA-A*31:01, multi-gene panels, and combinatorial pharmacogenomics tests. These tests are generally covered (with a few exceptions) as described in further detail below to increase safety in the use of specific medications by avoiding potentially harmful medications or doses.

Proposed LCD Posting Date

08/22/2019

Comment Period Start Date

10/07/2019

Comment Period End Date

11/21/2019

https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=38293

UnitedHealthcare®

UnitedHealthcare® Commercial
Medical Policy

PHARMACOGENETIC TESTING

Policy Number: 2019T0587E **Effective Date**: October 1, 2019

The use of pharmacogenetic Multi-Gene Panels to guide therapy decisions is proven and medically necessary for antidepressants and antipsychotics medication when ALL of the following criteria are met:

- The individual has a diagnosis of major depressive disorder or anxiety; **and**
- The individual has failed at least one prior medication to treat their condition; **and**
- The Multi-Gene Panel has no more than 15 relevant genes (refer to Table 1).

The use of pharmacogenetic Multi-Gene Panels for genetic polymorphisms for any other indication, including but not limited to pain management, cardiovascular drugs, anthracyclines, or polypharmacy, is unproven and not medically necessary for evaluating drug-metabolizer status due to insufficient evidence of efficacy.

Examples of these Panels include, but are not limited to the following:

- GeneSight® Analgesic
- GeneSight® ADHD
- SureGene Test
- Pain Medication DNA Insights®
- PharmacoDx

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Genomind Restores Drug Information to PGx Reports, But Only for Physicians

By Alex Philippidis - September 23, 2019 541

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Mental Health Advocacy Groups Appeal to FDA to Reconsider PGx Enforcement Activity

Sep 26, 2019 | staff reporter

Clinical OMICs

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Clinical Lab Association Urges FDA to Halt Crackdown on PGx Testing

HEALTH

STAT+

FDA warns testing companies: Don't tell patients how their DNA influences response to specific drugs

By REBECCA ROBBINS @rebeccadrobbins / AUGUST 28, 2019

ASSOCIATION FOR MOLECULAR PATHOLOGY
Education. Innovation & Improved Patient Care. Advocacy.
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- All health-related pharmacogenomic claims must have well-established clinical validity. The drug-gene association must be robust and supported by strong scientific evidence in the peer-reviewed literature, in the FDA-approved drug label, and/or in clinical practice guidelines, such as those created by CPIC.
- The pharmacogenomic testing provider must comply with the CLIA statute and regulations, as is required for all other clinical laboratory tests…
- The pharmacogenomic test report should be comprehendible by healthcare providers without medical genetics or pharmacogenomics training and include the interpretation of the findings, the significance of the results, as well as the limitations of the test.
- AMP strongly recommends that patients should not change their treatment plan without first talking to their healthcare provider.

AMP position: https://www.amp.org/AMP/assets/File/position-statements/2019/Best_Practices_for_PGx_9_4_2019.pdf?pass=98

NEWS

ACLA Deeply Concerned by FDA Actions on Pharmacogenetic Testing

September 18, 2019 Categories: *News, Featured News, ACLA Press Releases*

Agency actions limit clinical information for physicians and patients, undermine Congress and ongoing diagnostic reform efforts

Washington, D.C. – In response to the U.S. Food and Drug Administration (FDA)'s troubling actions against pharmacogenetic (PGx) testing, ACLA urged the agency to immediately reconsider and reverse its recent decisions in light of the significant harm and consequences to patient care. Taken together, FDA's actions appear to signal a move by the agency towards an outright ban of PGx testing developed and performed by laboratories, to the severe detriment of health care practitioners and patients.

Providers rely on PGx tests to identify genetic markers and clinically actionable information that can anticipate a pat based on well-documented scientific evidence. By helping providers pinpoint likely adverse drug reactions, PGx test significant costs associated with trial and error and supports a more efficient, patient-centered approach to care.

In a letter to the agency, ACLA points out that the FDA's approach to PGx enforcement will result in unprecedented By advancing regulatory action without public justification, rulemaking or stakeholder feedback, the agency's actions complications and costs for patients and the health system at large.

Highlights from the letter are included below.

- "ACLA is deeply concerned about FDA's actions, which will have the practical effect of taking away actionable inf health care professionals every day to make informed prescribing decisions. This will negatively impact patient c costs, especially in situations where there is not an FDA-cleared or approved alternative to a PGx test."
- "FDA's actions are not based on any new statutory authority, regulation, or even a guidance document."
- "Moreover, LDTs are not medical devices and in recent years ACLA has been engaged in ongoing discussions with FDA and Congress on enacting a new statutory framework for diagnostic regulation. Now, in the middle of those discussions, FDA has effectively banned a critical subset of LDTs. These actions not only undermine progress in developing a comprehensive legislative solution but also amount to an inappropriate form of backdoor regulation of LDTs."
- "FDA's actions have the practical effect of taking away valuable tools that physicians rely on for making informed prescribing decisions. Given that physicians will be forced to revert to older methodologies (such as try and fail, try and maybe succeed) in order to make prescribing decisions without actionable genomic information, it is likely that FDA's new policy will result in more patients receiving less than optimal medications or doses, with consequent safety and cost ramifications. Moreover, the Agency's actions threaten to bring the pace of innovation and investment in PGx testing to a halt."

Conclusion

FDA's actions have the practical effect of taking away valuable tools that physicians rely on for making informed prescribing decisions. Given that physicians will be forced to revert to older methodologies (such as try and fail, try and maybe succeed) in order to make prescribing decisions without actionable genomic information, it is likely that FDA's new policy will result in more patients receiving less than optimal medications or doses, with consequent safety and cost ramifications. Moreover, the Agency's actions threaten to bring the pace of innovation and investment in PGx testing to a halt.

For all of these reasons, ACLA requests a meeting to engage with FDA leadership on this topic. We look forward to a productive dialogue with FDA in the near future. In the meantime, should you have any questions about this letter, please feel free to reach me at 202-637-9466 or jkhani@acla.com.

ACLA letter to FDA: https://www.acla.com/wp-content/uploads/2019/09/ACLA-Letter-to-FDA-re_-PGx-Test-Policy-Sept-18-2019.pdf

Every patient deserves the GOLD STANDARD ...

Molecular Pathology Checklist

MOL.49615 **Report Criteria** **Phase II**

At a level appropriate for the particular test, the report includes a discussion of the limitations of the findings and the clinical implications of the detected mutation (or negative result) for complex disorders with regard to recessive or dominant inheritance, recurrence risk, penetrance, severity and other aspects of genotype-phenotype correlation.

NOTE: Because of the complexity of genotype-phenotype correlations for many genetic diseases, simply reporting a molecular genetic test as positive for a mutation is not acceptable since it conveys no information to the referring physician and patient as to the clinical ramifications of the result. Since major and often irreversible surgical or obstetric interventions may be initiated based on the test result, it is essential that the report convey the most current and accurate understanding of penetrance and recurrence risks.

REFERENCES

1) Clinical and Laboratory Standards Institute (CLSI). *Establishing Molecular Testing in Clinical Laboratory Environments*: CLSI document MM19-A (ISBN 1-56238-773-1). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2011.

http://webapps.cap.org/apps/docs/education/OnlineCourseContent/2014/TLTM/MOL04212014.PDF

Responses and actions

FDA takes new action to advance the development of reliable and beneficial genetic tests that can improve patient care

For Immediate Release: December 04, 2018

Genetic Database Recognition Decision Summary for

ClinGen Expert Curated Human Variant Data

Genetic Database Name: ClinGen Expert Curated Human Variant Data

Submission Number: Q181150

Summary of FDA Review to Support Recognition

The ClinGen Expert Curated Human Variant Data qualifies as a database per FDA's guidance document, "*Use of Public Human Genetic Variant Databases to Support Clinical Validity for Genetic and Genomic-based In Vitro Diagnostics*".

To support recognition of the Clinical Genome Resource (ClinGen) Expert Curated Human Variant Data, ClinGen submitted variant assertions and the evidence that supports them as well as the oversight and governance procedures for creating, maintaining, and expanding the currently available variant assertions within the scope described below. These assertions and procedures are publicly available. FDA evaluated whether these procedures provide reasonable assurance that the variant assertions made using the procedures are accurate and could be used as a source of valid scientific evidence in support of clinical validity of genetic and genomic-based tests in regulatory submissions. This evaluation was based upon whether ClinGen demonstrated conformance with the recommendations described in FDA's guidance document, "*Use of Public Human Genetic Variant Databases to Support Clinical Validity for Genetic and Genomic-based In Vitro Diagnostics*". Based upon the information reviewed, the FDA determined that the ClinGen Expert Curated Human Variant Data conforms to the recommendations described in the guidance. FDA's review of the information provided is described herein.

The FDA concludes that the ClinGen Expert Curated Human Variant Data procedures provide reasonable assurance that assertions from the database constitute valid scientific evidence that can be used to support clinical validity of genetic tests in future premarket submissions and therefore, FDA recognizes the ClinGen Expert Curated Human Variant Data for the scope described below.

Scope of Recognition

This recognition is for the ClinGen Expert Curated Human Variant Data variant classifications and the processes that support them for germline variants for hereditary disease where there is a high likelihood that the disease or condition will materialize given a deleterious variant (i.e., high penetrance).

Summary of Genetic Database Operations and Procedures to Support Recognition

ClinGen is a National Institutes of Health (NIH)-funded resource intended to aggregate, curate, and making publicly available information pertaining to the clinical significance of genotype-phenotype associations.

GUIDANCE DOCUMENT

Use of Public Human Genetic Variant Databases to Support Clinical Validity for Genetic and Genomic-Based In Vitro Diagnostics

Guidance for Stakeholders and Food and Drug Administration Staff

APRIL 2018

Download the Final Guidance Document

Update: Teri and Mary presenting PharmGKB and CPIC to CDER and CDRH to start process of "recognition" for each resource (Oct 2019)

This guidance document describes one part of FDA's efforts to create a flexible and adaptive regulatory approach to the oversight of next generation sequencing (NGS)-based tests. The goal of this effort is to help ensure patients receive accurate, reliable, and clinically meaningful test results, while promoting innovation in test development. This guidance document describes how publicly accessible databases of human genetic variants can serve as sources of valid scientific evidence to support the clinical validity of genotype-phenotype relationships in FDA's regulatory review of both NGS-based tests and genetic and genomic tests based on other technologies. Publicly accessible genetic databases may be useful to support the clinical validity of NGS tests as well as single gene or panel tests that use other technology.

PMC PERSONALIZED MEDICINE COALITION

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PMC: invited CPIC to present at their business meeting (Sept 2019); they stated they are interested in pursuing Collaborative Community with the FDA https://www.fda.gov/about-fda/cdrh-strategic-priorities-and-updates/collaborative-communities-addressing-healthcare-challenges-together

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GUIDANCE DOCUMENT

Clinical Decision Support Software

Guidance for Industry and Food and Drug Administration Staff

SEPTEMBER 2019

Download the Draft Guidance Document | Read the Federal Register Notice

Draft

Not for implementation. Contains non-binding recommendations.

This guidance is being distributed for comment purposes only.

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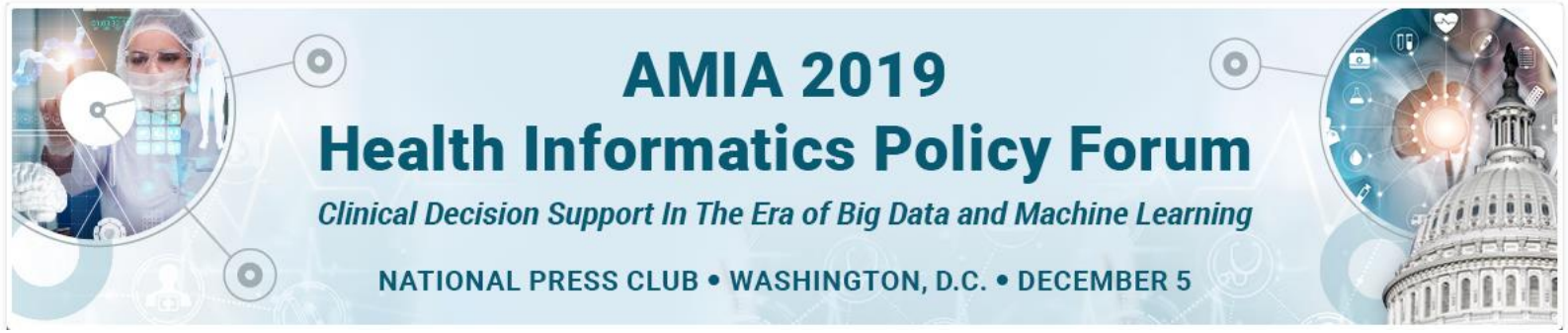
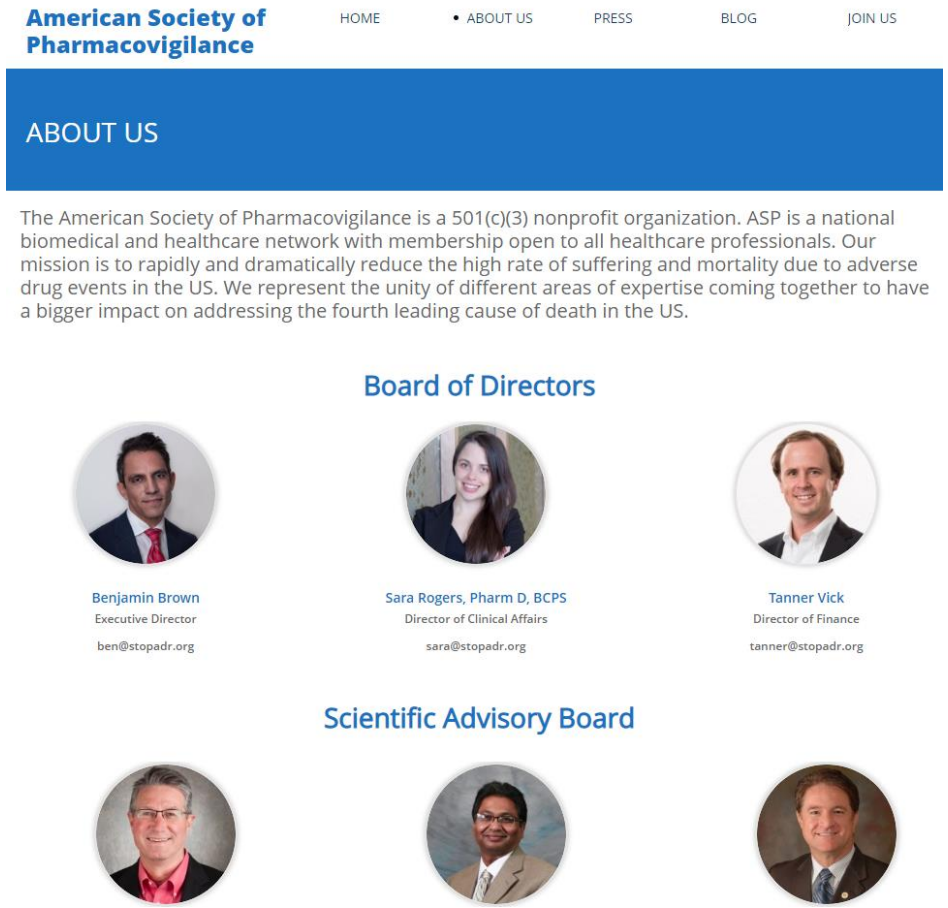


2:30 p.m. - 3:30 p.m.

Panel #3: Finding Consensus on FDA's Conceptual Cornerstone: Good Machine Learning Practices

- **Eileen Koski**, IBM Research
- **Bakul Patel**, Division of Digital Health, CDRH, Food and Drug Administration

Standardizing Laboratory Practices for Pharmacogenomics (STRIPE) Initiative via teleconference on Wednesday, October 16th at 11AM CST.



STRIPE
STANDARDIZING LABORATORY PRACTICES IN PHARMACOGENOMICS

STRIPE Initiative Launch Call RSVP

Name *

First Name Last Name

Title *

Company *

Phone Number *

Area Code - Phone Number

Email *

example@example.com

Are you planning to attend the STRIPE Initiative Launch via teleconference on Wednesday, October 16th at 11am CST? *

- [ ] Yes, I plan to attend.
- [ ] No, I cannot attend, but please send correspondence regarding the STRIPE Initiative.