Medical Coverage Policy

Effective Date..... 6/15/2020
Next Review Date..... 1/15/2021
Coverage Policy Number 0500

Pharmacogenetic Testing

Table of Contents

Related Coverage Resources

Genetics
Genetic Testing Collateral: Genetic Tests and Biomarkers File
Genetic Testing Collateral: Not Covered Single CPT® & HCPCS Code Tests
Cystic Fibrosis Transmembrance Conductance Regulator (CFTR) Modulators
Lomatipide Mesylate, Mipomersen Sodium
PCSK9 Inhibitors
Serological Testing for Inflammatory Bowel Disease

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations..

Coverage Policy

Many benefit plans limit coverage of genetic testing and genetic counseling services. Please refer to the applicable benefit plan language to determine benefit availability and terms, conditions and limitations of coverage for the services discussed in this Coverage Policy.

For additional information regarding coverage for specific genetic tests please refer to the Genetic Testing Collateral File.

General Coverage Principles

Medically Necessary

Pharmacogenetic testing (e. g., genotyping, mutation analysis) is considered medically necessary when EITHER of the following criteria is met (this list may not be all inclusive):

- All of the following:
    - The individual is a candidate for a targeted drug therapy associated with a specific gene biomarker or gene mutation
    - The results of the pharmacogenetic test will directly impact clinical decision-making
    - The testing method is considered to be scientifically valid to identify the specific gene biomarker or gene mutation
    - EITHER of the following:
        - Identification of the specific gene or biomarker for use with a specific drug target has been demonstrated to improve clinical outcomes for the individual's condition being addressed
        - Therapy with the targeted drug for the specific condition has been validated by a National Comprehensive Cancer Network (NCCN) category 1, 2A or 2B recommendation

- Identification of the gene biomarker is noted to be clinically necessary prior to initiating therapy with drug target as noted within the section heading "Indications and Usage" of the U.S. Food and Drug Administration (FDA)-approved prescribing label.

Not Medically Necessary

Pharmacogenetic screening in the general population is considered not medically necessary.

Overview

This Coverage Policy addresses pharmacogenetic testing. Pharmacogenetics is the study of gene variations within an individual's deoxyribonucleic acid (DNA) and how these differences influence an individual's response to medications. An individual's unique genetic makeup helps determine how he or she responds to a drug and whether or not side effects or adverse reactions may be experienced. Variations in genes may also cause an individual to metabolize a drug more quickly, more slowly or at the same rate as anticipated, based on dosage.

General Background

General Coverage Principles

Pharmacogenetics encompasses variation in genes that encode drug transporters, drug-metabolizing enzymes and drug targets, as well as specific genes related to the action of drugs. A slight variation in deoxyribonucleic acid (DNA) can result in a subtle change in a protein which translates into major differences in how the protein functions. The study of variations in DNA sequence as related to drug response is referred to as pharmacogenetic testing. A pharmacogenetic test is meant to guide treatment strategies, patient evaluations and decisions based on its ability to predict response to treatment in particular clinical contexts (Agency for Healthcare Research and Quality [AHRQ], 2010).

A particular variant is not always phenotype specific in that it may have a different impact depending on the drug in question. Racial and ethnic differences in the frequency and nature of genetic variants are also possible and should be recognized in translating outcomes from one population to another. The relation of a gene or gene biomarker and a drug target must be validated for each therapeutic indication in different racial and ethnic groups, as well as in different treatment and disease contexts (Kager and Evans, 2012).

Although genetics has an impact on genes related to inter-individual differences in drug response, it is only one of the many variables affecting these genes. Other factors include the characteristics of the condition for which the drug is prescribed, co-administration of other drugs, and non-genetic factors, including the individual's diet, weight, and smoking habits. Identification of gene variations may be clinically useful in a small number of drugs;

however, it may be insufficient in others to explain complex differences in metabolism, efficacy, and toxicity. The presence of polymorphisms alone may be a poor predictor of phenotype because of variability (Canadian Agency for Drugs and Technology in Health [CADTH], 2006).

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; however, laboratories offering such tests as a clinical service must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA) and must be licensed by CLIA for high-complexity testing. Additionally, laboratories in the U.S. should follow the College of American Pathology Guidelines. High complexity techniques used for pharmacogenetic testing include immunohistochemistry (IHC), fluorescent in situ hybridization (FISH), polymerase chain reaction (PCR) and microarray assays. According to the U.S. Food and Drug Administration (FDA), diagnostic tests that assay the presence of a particular pattern (e.g., single nucleotide polymorphism [SNP] set, haplotype pattern) should ideally be validated in a prospective clinical trial (2007).

An increasing number of multigene genotyping panels with the goals of detecting inter-individual differences in drug metabolism and response to a variety of drug targets are commercially available. The number of gene biomarkers and gene mutations and associated drug targets which are tested for vary widely between tests; some tests evaluate for a few biomarkers and associated drug targets while others may include hundreds of biomarkers within the test. Some multigene assays assess for the presence or absence of multiple biomarkers and provide lists of potential therapeutic agents, clinical trials and review of published literature associated with the biomarkers that are identified in the patient sample.

Clinical Utility

According to the Secretary's Advisory Committee on Genetic Testing ([SACGT], 1999-2000), the clinical use of a genetic test should be based on analytical validity (i.e., analytical sensitivity and specificity), and clinical validity (i.e., clinical sensitivity and specificity), and both positive and negative predictive value. Before a genetic test can be generally accepted in clinical practice, data must be collected to demonstrate the benefits and risks from both positive and negative results (i.e., the test must have clinical utility).

The clinical usefulness or utility of pharmacogenetic testing is the extent to which results of testing will impact clinical decision-making and improve health outcomes. Pharmacogenetic test results are meant to guide patient evaluation and treatment strategy and decisions based on the ability to predict response to treatment in particular clinical contexts, and to allow the clinician to predict an individual's response to specific pharmacotherapy, assist in making treatment choices, individualize drug dosages in order to maintain a consistent drug level in the body and avoid adverse reactions from overdose or suboptimal effects from under medication (Agency for Healthcare Research and Quality [AHRQ], 2010; Al-Goul, et al., 2008). The integration of genomic data in patient treatment requires evidence of consistency and size of measured effects, medication compliance and phenoconversion. The effects of ethnicity must be evaluated, especially in the context of global drug development and extrapolation of clinical trial genomic data from one population to another (Ehmann et al. 2014).

To definitively show that pharmacogenetic testing has value in clinical practice, it is not enough to demonstrate that drug response varies by genotype. Testing for the genotype and subsequently tailoring the treatment strategy based on genetic information should be more clinically effective and/or cost effective than treating an individual by an established treatment standard (Arnett, 2007).

When applied in a clinical setting, the information from these tests can potentially identify individual variability in drug response, including both effectiveness and toxicity. The individual for whom testing is proposed should be a candidate for a targeted drug therapy associated with a specific gene biomarker or gene mutation and results of testing must directly impact clinical decision making. The identification of the specific gene or biomarker for use with a specific drug target must also be demonstrated by published, peer-reviewed clinical trial data to improve clinical outcomes for an individual receiving that specific treatment and be considered scientifically valid to identify the biomarker.

For cancer-related conditions, clinical utility is established if there is a Category 1, 2A or 2B National Comprehensive Cancer Network™ [NCCN Guideline™] recommendation specific for the gene biomarker and associated drug target. Notation in the US Food and Drug Administration 'Indications and Usage' section of the

US Food and Drug Administration (FDA) prescribing label that identification of the gene biomarker is clinically necessary prior to prescribing of the drug target also establishes clinical utility for pharmacogenetic testing.

The National Comprehensive Cancer Network™ evidence grading system describes the level of evidence and the degree to which there is consensus for various treatment recommendations:

NCCN Category	Description
1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
2A	Based upon lower level of evidence, there is uniform NCCN consensus that the intervention is appropriate.
2B	Based upon lower-level of evidence, there is NCCN consensus that the intervention is appropriate.

US Food and Drug Administration (FDA)
The FDA considers the use of genomic information in drug labels either to require a genetic test for prescribing a drug, to recommend the use of a genetic test prior to drug therapy, or simply to provide information about the current knowledge of genomics that is relevant to drug therapy without the requirement or recommendation of a specific action. While the clinical utility of genotyping prior to treatment is not proven for all medications for which genomic information is included (Slavin, 2015), clinical utility is established when identification of a specific gene biomarker is noted to be clinically necessary prior to initiating therapy with a specific drug target as noted within the section heading “Indications and Usage” of the U.S. Food and Drug Administration (FDA)-approved prescribing label.

An FDA Safety Communication (2017) warns against the use of many genetic tests with unapproved claims to predict patient response to specific medications. The Communication’s intent was to alert patients and health care providers that for many genetic tests, claims to predict a patient's response to specific medications have not been reviewed by the FDA, and may not have the scientific or clinical evidence to support this use for most medications. Changing drug treatment based on the results from such a genetic test could lead to inappropriate treatment decisions and potentially serious health consequences for the patient. The FDA specifically notes the relationship between DNA variations and the effectiveness of antidepressant medication has never been established. According to the FDA, there are a limited number of cases for which at least some evidence does exist to support a correlation between a genetic variant and drug levels within the body, and this is described in the labeling of FDA cleared or approved genetic tests and FDA approved medications.

Literature Review
Increasingly, published, peer-reviewed scientific evidence regarding the clinical utility of pharmacogenetic testing informs on the ability of such testing to benefit health outcomes. Prospective clinical trials of standard management procedures compared with genetic test-directed management offers the highest level of evidence. Evidence may also be derived using banked samples from already-completed clinical trials; or by constructing an indirect chain of evidence linking test results to clinical outcome. To date, much of the existing research in the area of pharmacogenetic testing has been limited by study design, including uncontrolled and poorly defined case and control groups, presence of confounding variables, and the use of retrospective and non-blinded study protocols.

Although genome-wide association studies report inter-individual variability, high-quality, randomized controlled trial data demonstrating improved clinical outcomes are lacking. Many early phase clinical trials are exploratory, with no formal genomic hypothesis, and have small sample sizes that make it difficult to identify important gene variants influencing pharmacokinetics and pharmacodynamics (Lesko and Schmidt, 2014). However, clinical utility has been established for pharmacogenetic testing for a number of gene biomarkers and their specific drug targets.

Zeier et al., (2018) reviewed the evidence for several combinatorial pharmacogenetic test decision support tools whose potential utility to improve antidepressant treatment response or side effect burden has been evaluated in clinical settings. The authors note available literature suffers from publication bias, because some products garner more investment than do others, and questions about scientific integrity are inherent in studies conducted

by or reports authored by personnel with significant financial interests in the outcome. Although some of the preliminary published data sound promising, particularly with regard to theCYP450gene variants and side effect burden, we conclude that there is insufficient evidence to support widespread use at this point in time.

Wang et al. (2014) published results of a study evaluating the evidence that supports pharmacogenomic biomarker testing in drug labels and how frequently testing is recommended. Using guidelines published by the Evaluation of Genomic Applications in Practice and Prevention Working Group and FDA databases, the authors reviewed drug labels that described the use of a biomarker for reference to clinical validity and clinical utility. Of 119 notations in drug labels 36.1% provided evidence of clinical validity evidence while 15.1% provided evidence of clinical utility. Sixty-one labels (51.3%) made recommendations regarding clinical management based on the results of a biomarker test. Of these, 30.3% provided clinical utility data. A full description of supporting studies was included in 13 labels (10.9%). The authors noted that it may be premature to include biomarker recommendations in drug labels when data regarding patient outcomes are not available.

Pharmacogenetic testing is not currently recommended for general population screening. Clinical trials regarding the use of pharmacogenetic testing for screening in the general population are lacking in the published, peer-reviewed scientific literature and the role of such testing has not been established.

Professional Societies/ Organizations
While the NCCN has established recommendations for pharmacogenetic testing for a number of specific gene biomarkers and drug targets for cancer-related indications, there is limited published professional society consensus guideline support for pharmacogenetic testing for non-cancer-related conditions.

American Board of Internal Medicine Choosing Wisely
A statement by the American Society of Clinical Oncology recommends the following:

- Don't use cancer-directed therapy for solid tumor patients with the following characteristics: low performance status (3 or 4), no benefit from prior evidence-based interventions, not eligible for a clinical trial, and no strong evidence supporting the clinical value of further anti-cancer treatment.

The statement further notes cancer directed treatments are likely to be ineffective for solid tumor patients who meet the above stated criteria. Exceptions include patients with functional limitations due to other conditions resulting in a low performance status or those with disease characteristics (e.g., mutations) that suggest a high likelihood of response to therapy. Implementation of this approach should be accompanied with appropriate palliative and supportive care.

Centers for Medicare & Medicaid Services (CMS):

- National Coverage Determinations (NCDs): Pharmacogenomic Testing for Warfarin Response (90.1), last revised 8/3/2009. The Coverage Policy is broader in scope than the NCD. Refer to the CMS NCD table of contents link in the reference section.
- Local Coverage Determinations (LCDs): No Local Coverage Determinations found.

Use Outside of the US
No relevant statements.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s)

81226	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)
81232	DPYD (dihydropyrimidine dehydrogenase) (eg, 5-fluorouracil/5-FU and capecitabine drug metabolism), gene analysis, common variant(s) (eg, *2A, *4, *5, *6)
81235	EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)
81247	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (eg, A, A-)
81275	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; variants in exon 2 (eg, codons 12 and 13)
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (eg, codon 61, codon 146)
81306	NUDT15 (nudix hydrolase 15) (eg, drug metabolism) gene analysis, common variant(s) (eg, *2, *3, *4, *5, *6)
81315	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative
81316	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; single breakpoint (eg, intron 3, intron 6 or exon 6), qualitative or quantitative
81335	TPMT (thiopurine S-methyltransferase) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)
81346	TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (eg, tandem repeat variant)
81400	Molecular pathology procedure, Level 1 (eg, identification of single germline variant [eg, SNP] by techniques such as restriction enzyme digestion or melt curve analysis)
81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
81405	Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis)
0034U	TPMT (thiopurine S-methyltransferase), NUDT15 (nudix hydroxylase 15)(eg, thiopurine metabolism) gene analysis, common variants (ie, TPMT *2, *3A, *3B, *3C, *4, *5, *6, *8, *12; NUDT15 *3, *4, *5)
0037U	Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden
0070U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, common and select rare variants (ie, *2, *3, *4, *4N, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14A, *14B, *15, *17, *29, *35, *36, *41, *57, *61, *63, *68, *83, *xN)

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	**Description**
81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6)

ICD-10 CM Codes	**Description**
G35	Multiple sclerosis

Considered Not Medically Necessary:

CPT®* Codes	Description
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17)
81230	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22)
81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7)
81283	IFNL3 (interferon, lambda 3) (eg, drug response), gene analysis, rs12979860 variant
81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (eg, adverse drug reaction), gene analysis, common variant(s) (eg, *5)
81350	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (eg, irinotecan metabolism), gene analysis, common variants (eg, *28, *36, *37)
81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (eg, warfarin metabolism), gene analysis, common variant(s) (eg, -1639G>A, c.173+1000C>T)
81479†	Unlisted molecular pathology procedure
0028U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, copy number variants, common variants with reflex to targeted sequence analysis
0029U	Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis (ie, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, VKORC1 and rs12777823)
0030U	Drug metabolism (warfarin drug response), targeted sequence analysis (ie, CYP2C9, CYP4F2, VKORC1, rs12777823)
0031U	CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)(eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7)
0032U	COMT (catechol-O-methyltransferase))(eg, drug metabolism) gene analysis, c.472G>A (rs4680) variant
0033U	HTR2A (5-hydroxytryptamine receptor 2A), HTR2C (5-hydroxytryptamine receptor 2C) (eg, citalopram metabolism) gene analysis, common variants (ie, HTR2A rs7997012 [c.614-2211T>C], HTR2C rs3813929 [c.-759C>T] and rs1414334 [c.551-3008C>G])
0071U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, full gene sequence (List separately in addition to code for primary procedure)
0072U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D6-2D7 hybrid gene) (List separately in addition to code for primary procedure)
0073U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D7-2D6 hybrid gene) (List separately in addition to code for primary procedure)
0074U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, non-duplicated gene when duplication/multiplication is trans) (List separately in addition to code for primary procedure)
0075U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 5' gene duplication/multiplication) (List separately in addition to code for primary procedure)
0076U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 3' gene duplication/multiplication) (List separately in addition to code for primary procedure)
0078U	Pain management (opioid-use disorder) genotyping panel, 16 common variants (ie, ABCB1, COMT, DAT1, DBH, DOR, DRD1, DRD2, DRD4, GABA, GAL, HTR2A, HTTLPR, MTHFR, MUOR, OPRK1, OPRM1), buccal swab or other germline tissue sample, algorithm reported as positive or negative risk of opioid-use disorder
0173U	Psychiatry (ie, depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes (code effective 07/01/2020)

0175U	Psychiatry (eg, depression, anxiety), genomic analysis panel, variant analysis of 15 genes (code effective 07/01/2020)

†**Note: Considered Not Medically Necessary when used to report any non- covered genetic test for pharmacogenetics testing that does not have an assigned CPT/HCPCS code**

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
G9143	Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)

References

1. Abraham JE, Maranian MJ, Driver KE, Platte R, Kalmyrzaev B, Baynes C, Luccarini C, Earl HM, Dunning AM, Pharoah PD, Caldas C. CYP2D6 gene variants and their association with breast cancer susceptibility. Cancer Epidemiol Biomarkers Prev. 2011 Jun;20(6):1255-8.

2. Aithal GP, Day CP, Kesteven PJ, Daly AK. Association of polymorphisms in the cytochrome P450 CYP2C9 with warfarin dose requirement and risk of bleeding complications. Lancet. 1999 Feb 27;353(9154):717-9.

3. Al-Ghoul M, Valdes R Jr. Fundamentals of pharmacology and applications in pharmacogenetics. Clin Lab Med. 2008 Dec;28(4):485-97.

4. Amann JM, Lee JW, Roder H, Brahmer J, Gonzalez A, Schiller JH, Carbone DP. Genetic and proteomic features associated with survival after treatment with erlotinib in first-line therapy of non-small cell lung cancer in Eastern Cooperative Oncology Group 3503. J Thorac Oncol. 2010 Feb;5(2):16978.

5. American Society of Clinical Oncology. Practice and Guidelines. Clinical Practice Guidelines: American Society of Clinical Oncology Clinical Practice Guideline. Nov 21, 2018. Available at URL address: https://www.asco.org/practice-guidelines/quality-guidelines/guidelines

6. Anderson JL, Horne BD, Stevens SM, Grove AS, Barton S, Nicholas ZP, et al.; Couma-Gen Investigators. Randomized trial of genotype-guided versus standard warfarin dosing in patients initiating oral anticoagulation. Circulation. 2007 Nov 27;116(22):2563-70.

7. Anderson JL, Horne BD, Stevens SM, Woller SC, Samuelson KM, Mansfield JW, et al. A randomized and clinical effectiveness trial comparing two pharmacogenetic algorithms and standard care for individualizing warfarin dosing (CoumaGen-II). Circulation. 2012 Apr 24;125(16):1997-2005. Epub 2012 Mar 19.

8. Andreassen TN, Eftedal I, Klepstad P, Davies A, Bjordal K, Lundström S, Kaasa S, Dale O. Do CYP2D6 genotypes reflect oxycodone requirements for cancer patients treated for cancer pain? A cross-sectional multicentre study. Eur J Clin Pharmacol. 2012 Jan;68(1):55-64.

9. Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G; American College of Chest Physicians. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008 Jun;133(6 Suppl):160S-198S.

10. Aquilante CL, Langaee TY, Lopez LM, Yarandi HN, Tromberg JS, et al. Influence of coagulation factor, vitamin K epoxide reductase complex subunit 1, and cytochrome P450 2C9 gene polymorphisms on warfarin dose requirements. Clin Pharmacol Ther. 2006 Apr;79(4):291-302.

11. Bae JW, Choi CI, Lee HI, Lee YJ, Jang CG, Lee SY. Effects of CYP2C9*1/*3 and *1/*13 on the pharmacokinetics of losartan and its active metabolite E-3174. Int J Clin Pharmacol Ther. 2012 Sep;50(9):683-9.

12. Bakker PR, van Os J, van Harten PN. [The genetics of antipsychotic-related movement disorders]. Tijdschr Psychiatr. 2015;57(2):114-9.

13. Baudhuin LM, Highsmith WE, Skierka J, Holtegaard L, Moore BE, O'Kane DJ. Comparison of three methods for genotyping the UGT1A1 (TA)n repeat polymorphism. Clin Biochem. 2007 Jun;40(9-10):710-7.

14. Baudhuin LM, Langman LJ, O'Kane DJ. Translation of pharmacogenetics into clinically relevant testing modalities. Clin Pharmacol Ther. 2007 Oct;82(4):373-6.

15. Bauer T, Bouman HJ, van Werkum JW, Ford NF, ten Berg JM, Taubert D. Impact of CYP2C19 variant genotypes on clinical efficacy of antiplatelet treatment with clopidogrel: systematic review and meta-analysis. BMJ. 2011 Aug 4;343:d4588. doi: 10.1136/bmj.d4588.

16. Berm EJ, Hak E, Postma M4, Boshuisen M6 Breuning L, Brouwers JR, Dhondt T, Jansen PA, Kok RM, Maring JG, van Marum R, Mulder H, Voshaar RC, Risselada AJ, Venema H, Vleugel L, Wilffert B. Effects and cost-effectiveness of pharmacogenetic screening for CYP2D6 among older adults starting therapy with nortriptyline or venlafaxine: study protocol for a pragmatic randomized controlled trial (CYSCEtrial). Trials. 2015 Jan 31;16:37. doi: 10.1186/s13063-015-0561-0.

17. Bhatt DL, Pare G, Eikelboom JW, Simonsen KL, Emison ES, Fox, KA, et al. The relationship between CYP2C10 polymorphisms and ischaemic and bleeding outcomes in stable patients: the CHARISMA genetics study. Eur Heart J. 2012 Sep;33(17):2143-50.

18. Bradley P, Shiekh M, Mehra V, Vrbicky K, Layle S, Olson MC, et al. Improved efficacy with targeted pharmacogenetic-guided treatment of patients with depression and anxiety: A randomized clinical trial demonstrating clinical utility. J Psychiatr Res. 2018 Jan;96:100-107.

19. Brandl EJ, Tiwari AK, Zhou X, Deluce J, Kennedy JL, Müller DJ, Richter MA. Influence of CYP2D6 and CYP2C19 gene variants on antidepressant response in obsessive-compulsive disorder. Pharmacogenomics J. 2013 Apr 2.

20. Brown JT1, Bishop JR. Atomoxetine pharmacogenetics: associations with pharmacokinetics, treatment response and tolerability. Pharmacogenomics. 2015 Aug 28. [Epub ahead of print].

21. Byeon JY, Kim YH, Na HS, Jang JH, Kim SH, Lee YJ, Bae JW, Kim IS, Jang CG, Chung MW, Lee SY. Effects of the CYP2D6*10 allele on the pharmacokinetics of atomoxetine and its metabolites. Arch Pharm Res. 2015 Aug 9. [Epub ahead of print]

22. Cabaleiro T, Roman M, Ochoa D, Talegon M, Prieto-Perez R, Wojnicz A, Lopez-Rodriguez R, Novalbos J, Abad-Santos F. Evaluation of the relationship between sex, polymorphisms in cyp2c8 and cyp2c9 and pharmacokinetics of angiotensin receptor blockers. Drug Metab Dispos. 2013 Jan;41(1):224-9.

23. Caldwell MD, Berg RL, Zhang KQ, Glurich I, Schmelzer JR, Yale SH, et al. Evaluation of genetic factors for warfarin dose prediction. Clin Med Res. 2007 Mar;5(1):8-16.

24. Canadian Agency for Drugs and Technologies in Health. Issues in Emerging Health Technologies. Point-of-Care Phenotypic and Genetic Testing for Patients with Acute Coronary Syndrome. Issue 123 March 2013. Accessed Nov 21, 2018. Available at URL address: https://www.cadth.ca/point-care-phenotypic-and-genetic-testing-patients-acute-coronary-syndrome

25. Canadian Agency for Drugs and Technologies in Health (formerly known as Canadian Coordinating Office for Health Technology and Assessment). Palylyk-Colwell E. CYP450 genotyping for determining drug metabolizer status [Issues in emerging health technologies Issue 81] Ottawa. 2006. Accessed Nov 21, 2018. Available at URL address: https://www.cadth.ca/cyp450-genotyping-determining-drug-metabolizer-status-0

26. Candiotti KA, Yang Z, Rodriguez Y, Crescimone A, Sanchez GC, Takacs P, Medina C, Zhang Y, Liu H, Gitlin MC. The impact of CYP2D6 genetic polymorphisms on postoperative morphine consumption. Pain Med. 2009 Jul-Aug;10(5):799-805.

27. Caraco Y, Blotnick S, Muszkat M. CYP2C9 genotype-guided warfarin prescribing enhances the efficacy and safety of anticoagulation: a prospective randomized controlled study. Clin Pharmacol Ther. 2008 Mar;83(3):460-70.

28. Carlquist JF, McKinney JT, Nicholas ZP, Clark JL, Kahn SF, Horne BD, et al. Rapid melting curve analysis for genetic variants that underlie inter-individual variability in stable warfarin dosing. J Thromb Thrombolysis. 2007 Jul 29.

29. Caudle KE, Rettie AE, Whirl-Carrillo M, Smith LH, Mintzer S, Lee MT, Klein TE, Callaghan JT, Clinical Pharmacogenetics Implementation Consortium. Clinical pharmacogenetics implementation consortium guidelines for CYP2C9 and HLA-B genotypes and phenytoin dosing. Clin Pharmacol Ther. 2014 Nov;96(5):542-8.

30. Centers for Disease Control and Prevention (CDC). Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Evidence report. Recommendations from the EGAPP Working Group: can UGT1A1 genotyping reduce morbidity and mortality in patients with metastatic colorectal cancer treated with irinotecan? Genet Med. 2009 Jan;11(1):15-20. Accessed Nov 20, 2018. Available at URL address: https://www.cdc.gov/egappreviews/recommendations/index.html

31. Centers for Disease Control and Prevention (CDC). Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Recommendations from the EGAPP Working Group: testing for cytochrome P450 polymorphisms in adults with nonpsychotic depression treated with selective serotonin reuptake inhibitors. Genet Med. 2007 Dec;9(12):819-25. Accessed Nov 21, 2018. Available at URL address: https://www.cdc.gov/egappreviews/recommendations/index.html

Centers for Medicare & Medicaid Services (CMS). Pharmacogenomic Testing for warfarin response NCD 90.1. August 2009. Accessed Oct 5, 2019. Available at URL address: https://www.cms.gov/medicare-coverage-database/indexes/ncd-alphabetical-index.aspx?NCDId=23&ncdver=1&bc=AgAAgAAAAAAA&

32. Céspedes-Garro C, Jiménez-Arce G, Naranjo ME, Barrantes R, Llerena A; CEIBA.FP Consortium of the Ibero-American Network of Pharmacogenetics & Pharmacogenomics RIBEF. Ethnic background and CYP2D6 genetic polymorphisms in Costa Ricans. Rev Biol Trop. 2014 Dec;62(4):1659-71

33. Chou W, Yan F, Robbins-Weilert D, Ryder T, Liu W, Parrots C, et al. Comparison of Two CYP2D6 Genotyping Methods and Assessment of Genotype-Phenotype Relationships Clin Chem 2003;49:4:542–51.

34. Claudio-Campos K, Duconge J, Cadilla CL, Ruano G. Pharmacogenetics of drug-metabolizing enzymes in US Hispanics. Drug Metabol Personal Ther. 2015 Jun;30(2):87-105.

35. Collet JP, Hulot JS, Pena A, Villard E, Esteve JB, Silvain J, et al. Cytochrome P450 2C19 polymorphism in young patients treated with clopidogrel after myocardial infarction: a cohort study. Lancet. 2009 Jan 24;373(9660):309-17.

36. Cooper GM, Johnson JA, Langaee TY, Feng H, Stanaway IB, Schwarz UI, et al. A genome-wide scan for common genetic variants with a large influence on warfarin maintenance dose. Blood. 2008 Aug 15;112(4):1022-7.

37. Cresci S, Depta JP, Lenzini PA et al. Cytochrome p450 gene variants, race, and mortality among clopidogrel-treated patients after acute myocardial infarction. Circ Cardiovasc Genet. 2014 Jun;7(3):277-86. Epub 2014 Apr 24.

38. Crews KR, Gaedigk A, Dunnenberger HM, Leeder JS, Klein TE, Caudle KE, Haidar CE, Shen DD, Callaghan JT, Sadhasivam S, Prows CA, Kharasch ED, Skaar TC. Clinical Pharmacogenetics Implementation Consortium Guidelines for Cytochrome P450 2D6 Genotype and Codeine Therapy: 2014 Update. Clin Pharmacol Ther. 2014 Jan 23.

39. Cuisset T, Frere C, Poyet R, Quilici J, Gaborit B, Bali L, et al. Clopidogrel response: Head-to-head comparison of different platelet assays to identify clopidogrel non-responder patients after coronary stenting. Arch Cardiovasc Dis. 2010 Jan;101(1):39-45.

40. Dahabreh IJ, Moorthy D, Lamont JL, Chen ML, Kent DM, Lau J. Testing of CYP2C19 Variants and Platelet Reactivity for Guiding Antiplatelet Treatment [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Sep. Available from http://www.ncbi.nlm.nih.gov/books/NBK236984/

41. Daly AK, Cascorbi I. Opportunities and limitations: the value of pharmacogenetics in clinical practice. Br J Clin Pharmacol. 2014 Apr;77(4):583-6.

42. D'Empaire I, Guico-Pabia CJ, Preskorn SH. Antidepressant treatment and altered CYP2D6 activity: are pharmacokinetic variations clinically relevant? J Psychiatr Pract. 2011 Sep;17(5): 330-9.

43. de Leon J, et al. The CYP2D6 poor metabolizer phenotype may be associated with risperidone adverse drug reactions and discontinuation. J Clin Psychiatry. 2005 Jan;66(1):15-27.

44. Dezentje VO, Guchelaar HJ, Nortier JW, van de Velde CJ, Gelderblom H. Clinical implications of CYP2D6 genotyping in tamoxifen treatment for breast cancer. Clin Cancer res. 2009 Jan1;15(1):15-21.

45. Dickinson GL, Lennard MS, Tucker GT, Rostami-Hodjegan A. The use of mechanistic DM-PK-PD modeling to assess the power of pharmacogenetic studies -CYP2C9 and warfarin as an example. Br J Clin Pharmacol. 2007 Jul;64(1):14-26.

46. Dubovsky SL. The usefulness of genotyping cytochrome P450 enzymes in the treatment of depression. Expert Opin Drug Metab Toxicol. 2015 Mar;11(3):369-79. doi: 10.1517/17425255.2015.998996. Epub 2015 Jan 2.

47. Dunbar L, Miles W, Wheeler A, Sheridan J, Pulford J, Butler R. The CYP2D6 metaboliser status of patients prescribed risperidone for the treatment of psychosis. N Z Med J. 2009 Jun 5;122(1296):29-34.

48. Ehmann F, Caneva L, Papluca M. European Medicines Agency initiatives and perspectives on pharmacogenomics. Br J Clin Pharmacol. 2014 Apr; 77(4): 612–617.

49. Epstein RS, Moyer TP, Aubert RE, O'Kane DJ, Xia F, Verbrugge RR, et al. Warfarin Genotyping Reduces Hospitalization Rates Results From the MM-WES (Medco-Mayo Warfarin Effectiveness Study). J Am Coll Cardiol. 2010 Apr 7. [Epub ahead of print]

50. Ernst T, Erben P, Muller MC, Paschka P, Schenk T, Hoffmann J, et al. Haematologica. 2008a Feb;93(2):186-92.

51. Ernst T, Hoffmann J, Erben P, Hanfstein B, Leitner A, Hehlmann R, et al. ABL single nucleotide polymorphisms may masquerade as BCR-ABL mutations associated with resistance to tyrosine kinase in patients with chronic myeloid leukemia. Haematologica. 2008b Sep;93(9):1389-93.

52. Evrard A, Mbatchi L. Genetic polymorphisms of drug metabolizing enzymes and transporters: the long way from bench to bedside. Curr Top Med Chem. 2012;12(15):1720-9.

53. Fargher EA, Eddy C, Newman W, Qasim F, Tricker K, Elliot RA, et al. Patients' and healthcare professionals' views on pharmacogenetic testing and its future delivery in the NHS. Pharmacogenomics. 2007 Nov;8(11):1511-9.

54. Ferder NS, Eby CS, Deych E, Harris JK, Ridker PM, Milligan PE, et al. Ability of VKORC1 and CYP2C9 to predict therapeutic warfarin dose during the initial weeks of therapy. J Thromb Haemost. 2010;8(1):95-100.

55. Ferreira PG, Costa S, Dias N, Ferreira AJ, Franco F. Simultaneous interstitial pneumonitis and cardiomyopathy induced by venlafaxine. J Bras Pneumol. 2014 May-Jun;40(3):313-8.

56. Fleeman N, Martin Saborido C, Payne K, Boland A, Dickson R, Dundar Y, et al. The clinical effectiveness and cost-effectiveness of genotyping for CYP2D6 for management of women with breast cancer treated with tamoxifen: a systematic review. Health Technol Assess. 2011 Sep;15(33):1-102.

57. Flockhart DA, O'Kane D, Williams MS, Watson MS, Gage B, Gandolfi R, et al.; ACMG Working Group on Pharmacogenetic Testing of CYP2C9, VKORC1 Alleles for Warfarin Use. Pharmacogenetic testing of CYP2C9 and VKORC1 alleles for warfarin. Genet Med. 2008 Feb;10(2):139-50.

58. Fohner A, Muzquiz LI, Austin MA, Gaedigk A, Gordon A, Thornton T, Rieder MJ, Pershouse MA, Putnam EA, Howlett K, Beatty P, Thummel KE, Woodahl EL. Pharmacogenetics in American Indian populations: analysis of CYP2D6, CYP3A4, CYP3A5, and CYP2C9 in the Confederated Salish and Kootenai Tribes. Pharmacogenet Genomics. 2013 Aug;23(8):403-14.

59. Franchini M, Mengoli C, Cruciani M, Bonfanti C, Mannucci PM. Effects on bleeding complications of pharmacogenetic testing for initial dosing of vitamin K antagonists: a systematic review and meta-analysis. J Thromb Haemost. 2014 Sep;12(9):1480-7.

60. Franco V, Perucca E. CYP2C9 polymorphisms and phenytoin metabolism: implications for adverse effects. Expert Opin Drug Metab Toxicol. 2015 Aug; 11(8):1269-79.

61. Frere C, Cuisset T, Morange PE, Quicili J, Camion-Jau L, Suat N, et al. Effect of cytochrome p450 polymorphisms on platelet reactivity after treatment with clopidogrel in acute coronary syndrome. Am J Cardiol. 2008 Apr 15;101(8):1088-93.

62. Gaikwad T, Ghosh K, Shetty S. VKORC1 and CYP2C9 genotype distribution in Asian countries. Thromb Res. 2014 Sep;134(3):537-44.

63. Gage BF. Pharmacogenetics-based coumarin therapy. Hematology Am Soc Hematol Educ Program. 2006;:467-73.

64. Gage BF, Lesko LJ. Pharmacogenetics of warfarin: regulatory, scientific, and clinical issues. J Thromb Thrombolysis. 2007 Oct 1; [Epub ahead of print]

65. Gardiner SH, Begg EJ. Pharmacogenetics, drug-metabolizing enzymes, and clinical practice. Pharmacol Rev. 2006 Sep;58(3):521-90.

66. Ginsburg GS, Konstance RP, Allsbrook JS, Schulman KA. Implications of pharmacogenomics for drug development and clinical practice. Arch Intern Med. 2005 Nov 14;165(20):2331-6.

67. Gladding P, Webster M, Zeng I, Farrell H, Stewart J, Ruygrok P, et al. The pharmacogenetics and pharmacodynamics of clopidogrel response: an analysis of the PRINC (Plavix Response in Coronary Intervention) trial. JACC Cardiovasc Interv. 2008 Dec;1(6):620-7.

68. Goetz MP, Knox SK, Suman VJ, Rae JM, Safgren SL, Ames MM, et al. The impact of cytochrome P450 2D6 metabolism in women receiving adjuvant tamoxifen. Breast Cancer Res Treat. 2007 Jan;101(1):113-21.

69. Goetz MP, Sun JX, Suman VJ, Silva GO, Perou CM, Nakamura Y, Cox NJ, Stephens PJ, Miller VA, Ross JS, Chen D, Safgren SL, Kuffel MJ, Ames MM, Kalari KR, Gomez HL, Gonzalez-Angulo AM, Burgues O, Brauch HB, Ingle JN, Ratain MJ, Yelensky R. Loss of heterozygosity at the CYP2D6 locus in breast cancer: implications for germline pharmacogenetic studies. J Natl Cancer Inst. 2014 Dec 8;107(2).

70. Glowacki F, Lionet A, Buob D, Labalette M, Allorge D, Provôt F, et al. CYP3A5 and ABCB1 polymorphisms in donor and recipient: impact on Tacrolimus dose requirements and clinical outcome after renal transplantation. Nephrol Dial Transplant. 2011 Sep;26(9):3046-50.

71. Goetz MP, Rae JM, Suman VJ, Safgren SL, Ames MM, Visscher DW, et al. Pharmacogenetics of tamoxifen biotransformation is associated with clinical outcomes of efficacy and hot flashes. J Clin Oncol. 2005 Dec 20;23(36):9312-28.

72. Goetz MP, Suman VJ, Couch FJ, Ames MM, Rae JM, Erlander MG, et al. Cytochrome P450 2D6 and homebox 13/interleukin-17B receptor: combining inherited and tumor gene markers for prediction of tamoxifen resistance. Clin cancer Res. 2008 Sep 15;14(18):5864-8.

73. Gregorc V, Novello S, Lazzari C, Barni S, Aieta M, Mencoboni M, et al. Predictive value of a proteomic signature in patients with non-small-cell lung cancer treated with second-line erlotinib or chemotherapy
    a. (PROSE): a biomarker-stratified, randomised phase 3 trial. Lancet Oncol. 2014 Jun;15(7):713-21

74. Guilherme SK and Botton MR. Pharmacogenomics of warfarin in populations of African descent. Br J Clin Pharmacol. 2013 Feb;75(2);334-346.

75. Guisti B, Gori AM, Marcucci R, Saracini C, Sestini I, Paniccia R, et al. Relation of cytochrome P450 2C19 loss-of-function polymorphism to occurrence of drug-eluting coronary stent thrombosis. Am J Cardiol. 2009 Mar 15;103(6):806-11.

76. Gulseth MP, Grice GR, Dager WE. Pharmacogenomics of warfarin: uncovering a piece of the warfarin mystery. Am J Health Syst Pharm. 2009 Jan 15;66(2):123-33.

77. Haas DW, Ribaudo HJ, Kim RB, Tierney C, Wilkinson GR, Gulick RM, et al. Pharmacogenetics of efavirenz and central nervous system side effects: an Adult AIDS Clinical Trials Group study. AIDS. 2004 Dec 3;18(18):2391-400.

78. Hall-Flavin DK, Winner JG, Allen JD, Carhart JM, Proctor B, Snyder KA, Drews MS, Eisterhold LL, Geske J, Mrazek DA. Utility of integrated pharmacogenomics testing to support the treatment of major depressive disorder in a psychiatric outpatient setting. Pharmacogenet Genomics. 2013 Oct;23(10):535-48.

79. Hall-Flavin DK, Winner JG, Allen JD, Jordan JJ, Nesheim RS, Snyder KA, Drews MS, Eisterhold LL, Biernacka JM, Mrazek DA. Using a pharmacogenomic algorithm to guide the treatment of depression. Transl Psychiatry. 2012 Oct 16;2:e172.

80. Haufroid V, Hantson P. CYP2D6 genetic polymorphisms and their relevance for poisoning due to amfetamines, opioid analgesics and antidepressants. Clin Toxicol (Phila). 2015 Jul;53(6):501-10

81. Heller T, Kirchheiner J, Armstrong VW, Luthe H, Tzvetkov M, Brockmöller J, Oellerich M. AmpliChip CYP450 GeneChip: a new gene chip that allows rapid and accurate CYP2D6 genotyping. Ther Drug Monit. 2006 Oct;28(5):673-7.

82. Hertz DL and McLeod HL. Using Pharmacogene Polymorphism Panels to Detect Germline Pharmacodynamic Markers in Oncology. Clin Cancer Res May 15, 2014 20;2530

83. Hicks JK, Swen JJ, Thorn CF, Sangkuhl K, Kharasch ED, Ellingrod VL, et al. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clinical pharmacology and therapeutics. 2013;93(5):402-8. Epub 2013/03/15. doi: 10.1038/clpt.2013.2

84. Higashi MK, Veenstra DL, Kondo LM, Wittkowsky AK, Srinouanprachanh SL, Farin FM, Rettie AE. Association between CYP2C9 genetic variants and anticoagulation-related outcomes during warfarin therapy. JAMA. 2002 Apr 3;287(13):1690-8.

85. Higgins MJ, Stearns V. CYP2D6 polymorphismas and tamoxifen metabolism: clinical relevance. Curr Oncol Rep. 2010 Jan;12(1):7-15.

86. Hillman MA, Wilke RA, Yale SH, Vidaillet HJ, Caldwell MD, Glurich I, et al. A prospective, randomized pilot trial of model-based warfarin dose initiation using CYP2C9 genotype and clinical data. Clin Med Res. 2005 Aug;3(3):137-45.

87. Hirsh J, Fuster V, Ansell J, Halperin J. American Heart Association/American College of Cardiology Foundation Guide to Warfarin Therapy. Circulation. 2003;107:1692-711.

88. Holmes MV, Perel P, Shah T, Hingorani AD, Casas JP. CYP2C19 genotype, clopidogrel metabolism, platelet function, and cardiovascular events: a systematic review and meta-analysis. JAMA. 2011 Dec 28;306(24):2704-14.

89. Hologic, Inc.. The Invader® UGT1A1 Molecular assay. 2011. Accessed Mar 13, 2013. Available at URL address: http://www.invaderchemistry.com/invader_applications/invader-ugt1a1.html

90. Horne BD, Lenzini PA, Wadelius M, Jorgensen AL, Kimmel SE, Ridker PM, et al. Pharmacogenetic warfarin dose refinements remain significantly influenced by genetic factors after one week of therapy. Thromb Haemost. 2012 Feb;107(2):232-40. Epub 2011 Dec 21.

91. Hoskins JM, Goldberg RM, Qu P, Ibrahim JG, McLeod HL. UGT1A1*28 genotype and irinotecan-induced neutropenia: dose matters. J Natl Cancer Inst. 2007 Sep 5;99(17):1290-5.

92. Huang SW, Chen HS, Wang XQ, Huang L, Xu DL, Hu XJ, et al. Validation of VKORC1 and CYP2C9 genotypes on interindividual warfarin maintenance dose: a prospective study in Chinese patients. Pharmacogenet Genomics. 2009 Mar;19(3):226-34.

93. Hughes T, Deininger M, Hochhaus A, Branford S, Radich J, Kaeda J, et al. Monitoring CML patients responding to treatment with tyrosine kinase inhibitors: review and recommendations for harmonizing current methodology for detecting BCR-ABL transcripts and kinase domain mutations and for expressing results. Blood. 2006 Jul 1;108(1):28-37.

94. Hulot JS, Cullot JP, Cayla G, Silvain J, Allanic F, Bellemain-Appaix A, et al. CYP2C19 but not PON1 genetic variants influence clopidogrel pharmacokinetics, pharmacodynamics, and clinical efficacy in post-myocardial infarction patients. Circ Cardiovasc Interv. 2011 Oct 1;4(5):422-8.

95. Hulot JS, Cullot JP, Silvain J, Pena A, Bellemain-Appaix A, Barthelemy O, et al. Cardiovascular risk in clopidogrel-treated patients according to cytochrome P450 2C19*2 loss-of-function allele or proton pump inhibitor coadministration: a systematic meta-analysis. J Am Coll Cardiol. 2010 Jul 6;56(2):134-43.

96. Hu ZY, Yu Q, Pei Q, Guo C. Dose-dependent association between UGT1A1*28 genotype and irinotecan-induced neutropenia: low doses also increase risk. Clin Cancer Res. 2010 Aug 1;16(15):3832-42.

97. Hu ZY, Yu Q, Zhao YS. Dose-dependent association between UGT1A1*28 polymorphism and irinotecan-induced diarrhea: a meta-analysis. Eur J Cancer. 2010 Jul;46(10):1856-65.

98. Ingelman-Sundberg M. Pharmacogenetic biomarkers as tools for improved drug therapy; emphasis on the cytochrome P450 system. Biochem Biophy Res Commun. 2010 May 21;396(1):90-4.

99. Ingelman-Sundberg, Rodriguez-Antona C. Pharmacogenetics of drug-metabolizing enzymes: implications for a safer and more effective drug therapy. Philos Trans R Soc Lond B Biol Sci. 2005 Aug 29;360(1460):1563-70.

100. Ingelman-Sundberg M. Pharmacogenetics of cytochrome P450 and its applications in drug therapy: the past, present and future. Trends Pharmacol Sci.2004 Apr;25(4):193-200.

101. International Warfarin Pharmacogenetics Consortium, Klein TE, Altman RB, Eriksson N, Gage BF, Kimmel SE, Lee MT, et al. Estimation of the warfarin dose with clinical and pharmacogenetic data. N Engl J Med. 2009 Feb 19;360(8):753-64.

102. Joffe HV, Xu R, Johnson FB, Longtine J, Kucher N, Goldhaber SZ. Warfarin dosing and cytochrome P450 2C9 polymorphisms. Thromb Haemost. 2004 Jun;91(6):1123-8.

103. Johnson JA, Cavallari LH, Beitelshees AL, Lewis JP, Shuldiner AR, Roden DM. Pharmacogeneomics: application to the management of cardiovascular disease. Clin Pharmacol Ther. 2011 Oct;90(4):519-31.

104. Johnson JA, Gong L, Whirl-Carillo M, Gage BF, Scott SA, Stein CM, et al. Clinical Pharmacogenetics implementation consortium guidelines for CYP2C9 and VKORC1 genotypes and warfarin dosing. Clin Pharmacol Ther. 2011 Oct;90(4):625-9.

105. Jurgens G, Rasmussen HB, Werge T, Dalhoff K, Nordentoft M, Andersen SE. Does the medication pattern reflect the CYP2D6 genotype in patients with diagnoses within the schizophrenic spectrum? J Clin Psychopharmacol. 2012 Feb;32(1):100-5.

106. Kamali F. Genetic influences on the response to warfarin. Curr Opin Hematol. 2006 Sep;13(5):357-61.

107. Kamali F, Pirmohamed M. The future prospects of pharmacogenetics in oral anticoagulation therapy. Br J Clin Pharmacol. 2006 Jun;61(6):746-51.

108. Kangelaris KN, Bent S, Nussbaum RL, Garcia DA, Tice JA. Genetic testing before anticoagulation? A systematic review of pharmacogenetic dosing of warfarin. J Gen Intern Med. 2009 May;24(5):656-64.

109. Khoury MJ. Dealing with the evidence dilemma in genomics and personalized medicine. Clin Pharmacol Ther. 2010 Jun;87(6):635-8.

110. Khoury MJ, Rich EC, RandhawaG, Teutsch SM, Niederhuber J. Comparative effectiveness research and genomic medicine: an evolving partnership for 21st century medicine. Genet Med. 2009 Oct;11(10):707-11.

111. Kim DH, Sriharsha L, Xu W, Kamel-Reid S, Liu X, Simovitch K, et al. Clinical relevance of a pharmacogenetic approach using multiple candidate genes to predict response and resistance to imatinib therapy in chronic myeloid leukemia. Clin Cancer Res. 2009 Jul 15;15(14):4750-8.

112. Kim TD, Turkman S, Schwartz M, Koca G, Nogai H, Bommer C, et al. Impact of additional chromosomal aberrations and BCR-ABL kinase domain mutations on the response to nilotinib in Philadelphia chromosome-positive chronic myeloid leukemia. Haematologic. 2010 Apr;95(4):582-8. Epub 2009 Dec 16.

113. King CR, Porche-Sorbet RM, Gage BF, Ridker PM, Renaud Y, Phillips MS, Eby C. Performance of commercial platforms for rapid genotyping of polymorphisms affecting warfarin dose. Am J Clin Pathol. 2008 Jun;129(6):876-83.

114. Kitzmiller JP, Groen DK, Phelps MA, Sadee W. Pharmacogenomic testing: relevance in medical practice: why drugs work in some patients but not in others. Cleve Clin J Med. 2011 Apr;78(4):243-57.

115. Kiyotani K, Mushiroda T, Sasa M, Bando Y, Sumitomo I, Hosono N, et al. Impact of CYP2D6*10 on recurrence-free survival in breast cancer patients receiving adjuvant tamoxifen therapy. Cancer Sci. 2008 May;99(5):995-9.

116. Kringen MK, Haug KB, Grimholt RM, Stormo C, Narum S, Opdal MS, et al. Genetic variation of VKORC1 and CYP4F2 genes related to warfarin maintenance dose in patients with myocardial infarction. J Biomed Biotechnol. 2011;2011:739-751.

117. Krishna V, Diamond GA, Kaul S. The role of platelet reactivity and genotype testing in the prevention of atherothrombotic cardiovascular events remains unproven. Circulation. 2012 Mar 13;125(10):1288-303.

118. Krynetskiy E, McDonnell P. Building individualized medicine: prevention of adverse reactions to warfarin therapy. J Pharmacol Exp Ther. 2007 Aug;322(2):427-34.

119. Laboratory Corporation of America. Tamoxifen CYP2D6 genotype-a technical review. ©2018 Laboratory Corporation of America® Holdings. Accessed Nov 20, 2018. Available at URL address: https://www.labcorp.com/

120. Lash TL, Cronin-Fenton D, Ahern TP, Rosenberg CL, Lunetta KL, Silliman RA, Garne JP, Sorensen HT, Hellberg Y, Christensen M, Pedersen L, Hamilton-Dutoit S. CYP2D6 inhibition and breast cancer recurrence in a population-based study in Denmark. J Natl Cancer Inst. 2011 Mar 16;103(6):489-500.

121. Lamba JK, Lin YS, Schuetz EG, Thummel KE. Genetic contribution to variable human CYP3A-mediated metabolism. Adv Drug Deliv Rev. 2002 Nov 18;54(10):1271-94.

122. Langley MR, Booker JK, Evans JP, McLeod HL, Weck KE. Validation of clinical testing for warfarin sensitivity: comparison of CYP2C9-VKORC1 genotyping assays and warfarin-dosing algorithms. J Mol Diagn. 2009 May;11(3):216-25.

123. Lassen D, Damkier P, Brøsen K. The Pharmacogenetics of Tramadol. Clin Pharmacokinet. 2015 Aug;54(8):825-36. doi: 10.1007/s40262-015-0268-0.

124. Lee JM, Park S, Shinn DJ, Choi D, Shim CY, Yo YG, et al. Relation of genetic polymorphisms in the cytochrome P450 gene with clopidogrel resistance after drug-eluting stent implantations in Koreans. Am J Cardiol. 2009 Jul 1;104(1):46-51.

125. Lefevre F, Goodman SN, Piper MA. Pharmacogenetic testing for warfarin dosing still awaits validation. J Am Coll Cardiol. 2011 Feb 8;57(6):756

126. Lenzini P, Wadelius M, Kimmel S, Anderson JL, Jorgenson AL, Pirohamed M, et al. Integration of genetic, clinical and INR data to refine warfarin dosing. Clin Pharmacol Ther. 2010 May;87(5):572-8.

127. Lesko LJ, Schimdt S. Clinical implementation of genetic testing in medicine: a US regulatory science perspective. Br J Clin Pharmacol. 2014 Apr; 77(4): 606–611.

128. Limdi NA, McGwin G, Goldstein JA, Beasley TM, Arnett DK, Adler BK, et al. Influence of CYP2C9 and VKORC1 1173C/T Genotype on the Risk of Hemorrhagic Complications in African-American and European-American Patients on Warfarin. Clin Pharmacol Ther. 2007 Jul 25.

129. Limdi NA, Veenstra DL. Warfarin pharmacogenetics. Pharmacotherapy. 2008 Sep;28(9):1084-97.

130. Lindh JD, Lundgren S, Holm L, Alfredsson L, Rane A. Several-fold increase in risk of overanticoagulation by CYP2C9 mutations. Clin Pharmacol Ther. 2005 Nov;78(5):540-50.

131. Linares OA, Daly D, Linares AD, Stefanovski D, Boston RC. Personalized oxycodone dosing: using pharmacogenetic testing and clinical pharmacokinetics to reduce toxicity risk and increase effectiveness. Pain Med. 2014 May;15(5):791-806.

132. Lorenzini K, Calmy A, Ambrosioni J, Assouline B, Daali Y, Fathi M, Rebsamen M, Desmeules J, Samer CF. Serotonin syndrome following drug-drug interactions and CYP2D6 and CYP2C19 genetic polymorphisms in an HIV-infected patient. AIDS. 2012 Nov 28;26(18):2417-8.

133. Ma JD, Lee KC, Kuo GM. Clinical application of pharmacogenomics. J Pharm Pract. 2012 Aug;25(4):417-27

134. MacPhee IA, Holt DW. A pharmacogenetic strategy for immunosuppression based on the CYP3A5 genotype. Transplantation. 2008 Jan 27;85(2):163-5.

135. Maruthur NM, Gribble MO, Bennett WL, Bolen S, Wilson LM, Balakrishnan P, Sahu A, Bass E, Kao WH Clark JM. The pharmacogenetics of type 2 diabetes: a systematic review. Diabetes Care. 2014;37(3):876-86.

136. McClain MR, Palomaki GE, Piper M, Haddow JE; Commissioned by ACMG. A Rapid ACCE Review of CYP2C9 and VKORC1 Allele Testing to Inform Warfarin Dosing in Adults at Elevated Risk for Thrombotic Events to Avoid Serious Bleeding. Feb 2008. Accessed Nov 21, 2017. Available at URL address: https://www.acmg.net/docs/Resources/Warfarin_CYP_VKOR_ACCE_review_8.21.07.pdf?hkey=6e8df859-fbf5-4bea-b5e4-dc482181e558

137. McKinnon RA, Ward MB, Sorich MJ. A critical analysis of barriers to the clinical implementation of pharmacogenomics. Ther Clin Risk Manag. 2007 Oct;3(5):751-59.

138. McMillin GA, Melis R, Wilson A, Strong MB, Wanner NA, Vinik RG, et al. Gene-based warfarin dosing compared with standard of care practices in an orthopedic surgery population: a prospective, parallel cohort study. Ther Drug Monit. 2010 Jun;32(3):338-45.

139. Mega JL, Close SL, Wiviott SD, Shen L, Hockett RD, Brandt JT, et al. Cytochrome P450 genetic polymorphisms and the response to prasurgrel: relationship to pharmacokinetic, pharmacodynamic and clinical outcomes. Circulation. 2009 May 19;119(19):2553-60.

140. Mega JL, Close SL, Wiviott SD, Shen L, Hockett RD, Brandt JT, et al. Cytochrome p-450 polymorphisms and response to clopidogrel. N Engl J Med. 2009 Jan 22;360(4):354-62.

141. Mega JL, Hochholzer W, Frelinger AL 3rd, Kluk MJ, Angiolillo DJ, Kereiakes DJ, et al. Dosing clopidogrel based on CYP2C19 genotype and the effect on platelet reactivity in patients with stable cardiovascular disease. JAMA. 2011 Nov 23;306(20):2221-8.

142. Mega JL, Simon T, Collet JP, Anderson JL, Antman EM, Bliden K, et al. reduced-function CYP2C19 genotype and risk of adverse clinical outcomes among patients treated with clopidogrel predominantly for PCI-a meta-analysis. JAMA. 2010 Oct 27;304(16):1821-30.

143. Mega JL, Walker JR, Ruff CT, Vandell AG, Nordio F, Deenadayalu N, Murphy SA, Lee J, Mercuri MF, Giugliano RP, Antman EM, Braunwald E, Sabatine MS. Genetics and the clinical response to warfarin and edoxaban: findings from the randomised, double-blind ENGAGE AF-TIMI 48 trial. Lancet. 2015 Jun;385(9984):2280-7.

144. Mehta R, Kelleher D, Preece A, Hughes S, Crater G, et al. Effect of verapamil on systemic exposure and safety of umeclidinium and vilanterol: a randomized and open-label study. Int J Chron Obstruct Pulmon Dis. 2013;8:159-67. Epub 2013 Mar 27.

145. Millican EA, Lenzina PA, Milligan PE, Grosso L, Eby C, Devch E, et al. Genetic-based dosing in orthopedic patients beginning warfarin therapy. Blood. 2007 Sep 1;110(5):1511-5.

146. Monte AA, Heard KJ, Campbell J, Hamamura D, Weinshilboum RM, Vasiliou V. The effect of CYP2D6 drug-drug interactions on hydrocodone effectiveness. Acad Emerg Med. 2014 Aug;21(8):879-85

147. Morrow PK, Serna R, Broglio K, Pusztai L, Nikoloff DM, Hillman GR, Fontecha M, Li R, Michaud L, Hortobagyi G, Gonzalez-Angulo AM. Effect of CYP2D6 polymorphisms on breast cancer recurrence. Cancer. 2012 Mar 1;118(5):1221-7.

148. Moyer TP, O'Kane DJ, Baudhuin LM, Wiley CL, Fortini A, Fisher PK, et al. Warfarin sensitivity genotyping: a review of the literature and summary of patient experience. Mayo Clin Proc. 2009 Dec;84(12):1079-94.

149. Nakamura A, Mihara K, Nemoto K, Nagai G, Kagawa S, Suzuki T, Kondo T. Lack of correlation between the steady-state plasma concentrations of aripiprazole and haloperidol in Japanese patients with schizophrenia. Ther Drug Monit. 2014 Dec;36(6):815-8.

150. National Center for Biotechnology Information (NCBI). U.S. National Library of Medicine. Genetic Testing Registry. Accessed Nov 20, 2018. Available at URL address: http://www.ncbi.nlm.nih.gov/gtr/genes/

151. National Comprehensive Cancer Network® (NCCN). NCCN GUIDELINES™ Clinical Guidelines in Oncology™. ©National Comprehensive Cancer Network, Inc 2018, All Rights Reserved. Accessed Nov 20, 2018. Available at URL address: https://www.nccn.org/

152. National Institute for Health Research (NIHR). The clinical effectiveness and cost-effectiveness of testing for cytochrome P450 polymorphisms in patients with schizophrenia treated with antipsychotics: a systematic review and economic evaluation. Health Technol Assess. 2010 Jan;14(3):1-157, iii. Accessed Nov 20, 2018. Available at URL address: https://www.journalslibrary.nihr.ac.uk/search/#/?search=P450%20polymorphisms%20in%20patients%20with%20schizophrenia%20&sitekit=true&indexname=full-index&task=search&selected_facets=

153. National Institute for Health Research (NIHR). [UK] The clinical effectiveness and cost-effectiveness of genotyping for CYP2D6 for the management of women with breast cancer treated with tamoxifen: a systematic review. Health Technol Assess 2011;15(33):1–102. Accessed Nov 20, 2018. Available at URL address: https://www.journalslibrary.nihr.ac.uk/search/#/?search=CYP2D6&sitekit=true&indexname=full-index&task=search&selected_facets=

154. Ngedwa S. Pharmacogenomics and warfarin therapy [Issues in emerging health technologies issue 104]. Ottawa: Canadian Agency for Drugs and Technology in Health; 2007.

155. Oake N, Fergusson DA, Forster AJ, van Walraven C. Frequency of adverse events in patients with poor anticoagulation: a meta-analysis. CMAJ. 2007 May 22;176(11):1589-94.

156. Ong FS, Deignan JL, Kuo JZ, Bernstein KE, Rotter JI, Grody WW, et al. Clinical utility of pharmacogenetic biomarkers in cardiovascular therapeutics: a challenge for clinical implementation. Pharmacogenomics. 2012 Mar;13(4):465-75.

157. Palomaki GE, Bradley LA, Douglas MP, Kolor K, Dotson WD, Can UGT1A1 genotyping reduce morbidity and mortality in patients with metastatic colorectal cancer treated with irinotecan? An evidence-based review. Genet Med. 2009 Jan;11(1):21-34.

158. Papanastasopoulos P and Stebbing J. Molecular Basis of 5-Fluorouracil-related Toxicity: Lessons from Clinical Practice. Anticancer ResearchApril 2014 vol. 34 no. 41531-1535

159. Pare G, Meta SR, Yusuf S, Anand SS, Connolly SJ, Hirsh J, et al. Effects of CYP2C19 genotype on outcomes of clopidogrel treatment. N Engl J Med. 2010 Oct 28;363918):1704-14.

160. Park HS, Choi JY, Lee MJ, Park S, Yeo CW, Lee SS, Shin JG, Park BW. Association between genetic polymorphisms of CYP2D6 and outcomes in breast cancer patients with tamoxifen treatment. J Korean Med Sci. 2011 Aug;26(8):1007-13.

161. Pena A, Collet JP, Hullot JS, Silvain J, Barthelemy O, Beygui F, et al. Can we override clopidogrel resistance? Circulation. 2009 Jun 2;119(21):2854-7.

162. Peyvandi F, Spreafico M, Siboni SM, Moia M, Mannucci PM. CYP2C9 genotypes and dose requirements during the induction phase of oral anticoagulant therapy. Clin Pharmacol Ther. 2004 Mar;75(3):198-203.

163. Potkin SG, Preskorn S, Hochfeld M, Meng X. A thorough QTc study of 3 doses of iloperidone including metabolic inhibition via CYP2D6 and/or CYP3A4 and a comparison to quetiapine and ziprasidone. J Clin Psychopharmacol. 2013 Feb;33(1):3-10.

164. Province MA, Goetz MP, Brauch H, Flockhart DA, Hebert JM, Whaley R, et al. CYP2D6 genotype and adjuvant tamoxifen: meta-analysis of heterogeneous study populations. Clin Pharmacol Ther. 2014Feb;95(2):216-27.

165. Prows CA, Zhang X, Huth MM, Zhang K, Saldaña SN, Daraiseh NM, Esslinger HR, Freeman E, Greinwald JH, Martin LJ, Sadhasivam S. Codeine-related adverse drug reactions in children following tonsillectomy: a prospective study. Laryngoscope. 2014 May;124(5):1242-50. doi: 10.1002/lary.24455. Epub 2013 Nov 13.

166. Qasim A, Seery J, Buckley M, Morain CO. TPMT in the treatment of inflammatory bowel disease with azathioprine. Gut. 2003;52(5):767.

167. Rae JM, Drury S, Hayes DF, Stearns V, Thibert JN, Haynes BP, et al. CYP2D6 and UGT2B7 genotype and risk of recurrence in tamoxifen-treated breast cancer patients. J Natl Cancer Inst. 2012 Mar 21;104(6):452-60.

168. Ramón Y Cajal T, Altés A, Paré L, Del Rio E, Alonso C, Barnadas A, Baiget M. Impact of CYP2D6 polymorphisms in tamoxifen adjuvant breast cancer treatment. Breast Cancer Res Treat. 2010 Jan;119(1):33-8. Epub 2009 Feb 3.

169. Rebsamen MC, Desmeules J, Daali Y, Chiappe A, Diemand A, Rey C, et al. The AmpliChip CYP450 test: cytochrome P450 2D6 genotype assessment and phenotype prediction. Pharmacogenomics J. 2009 Feb;9(1):34-41.

170. Regan MM, Leyland-Jones B, Bouzyk M, Pagani O, Tang W, Kammler R, et al. CYP2D6 genotype and tamoxifen response in postmenopausal women with endocrine-responsive breast cancer: the breast international group 1-98 trial. J Natl Cancer Inst. 2012 Mar 21;104(6):441-51.

171. Rettie AE, Tai G. The pharmocogenomics of warfarin: closing in on personalized medicine. Mol Interv. 2006 Aug;6(4):223-7.

172. Rieder MJ, Reiner AP, Gage BF, Nickerson DA, Eby CS, McLeod HL, et al. Effect of VKORC1 haplotypes on transcriptional regulation and warfarin dose. N Engl J Med. 2005 Jun 2;352(22):2285-93.

173. Rietveld L, van der Hoek T, van Beek MH, Schellekens AF. Familial liability for metoprolol-induced psychosis. Gen Hosp Psychiatry. 2015 Jun 25. pii: S0163-8343(15)00153-X

174. Robarge J, Fletcher R, Nguyen, A, Thorn CF. Pharmacogenomics Knowledge Base. ©2001-2017 PharmGKB. Accessed Nov 20, 2017. Available at URL address: https://www.pharmgkb.org

175. Rochat B. Role of cytochrome P450 activity in the fate of anticancer agents and in drug resistance: focus on tamoxifen, paclitaxel, and imatinib metabolism. Clin Pharmacokinet. 2005;44(4):349-66.

176. Roses AD. Pharmacogenetics. Hum Mol Genet. 2001 Oct 1;10(20):2261-7.

177. Ruddy KJ, Desantis SD, Gelman RS, Wu AH, Punglia RS, Mayer EL, Tolaney SM, Winer EP, Partridge AH, Burstein HJ. Personalized medicine in breast cancer: tamoxifen, endoxifen, and CYP2D6 in clinical practice. Breast Cancer Res Treat. 2013 Oct;141(3):421-7

178. Sacco K, Grech G. Actionable pharmacogenetic markers for prediction and prognosis in breast cancer. EPMA J. 2015 Jul 22;6(1):15. doi: 10.1186/s13167-015-0037-z. eCollection 2015.

179. Sanderson S, Emery J, Higgins J. CYP2C9 gene variants, drug dose, and bleeding risk in warfarin-treated patients: a HuGEnet systematic review and meta-analysis. Genet Med. 2005 Feb;7(2):97-104.

180. Samer CF, Daali Y, Wagner M, Hopfgartner G, Eap CB, Rebsamen MC, et al. Genetic polymorphisms and drug interactions modulating CYP2D6 and CYP3A activities have a major effect on oxycodone analgesic efficacy and safety. Br J Pharmacol. 2010 Jun;160(4):919-30.

181. Satoh T, Ura T, Yamada Y, Yamazaki K, Tsujinaka T, Munakata M, Nishina T, Okamura S, Esaki T, Sasaki Y, Koizumi W, Kakeji Y, Ishizuka N, Hyodo I, Sakata Y. Genotype-directed, dose-finding study of irinotecan in cancer patients with UGT1A1*28 and/or UGT1A1*6 polymorphisms. Cancer Sci. 2011 Oct;102(10):1868-73.

182. Scott SA, Sangkuhl K, Stein CM, Hulot J-S, Mega JL, Roden DM, Klein TE, Sabatine MS, Johnson JA, Shuldiner AR. Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C19 Genotype and Clopidogrel Therapy: 2013 Update. Clin Pharmacol Ther. 2013 Sep;94(3):317-23. Epub 2013 May 22.

183. Schroth W, Goetz MP, Hamann U, Fasching PA, Schmidt M, Winter S, et al. Association between CYP2D6polymorphisms and outcomes among women with early stage breast cancer treated with tamoxifen. JAMA. 2009 Oct 7;302(13):1429-36.

184. Schroth W, Hamann U, Fasching PA, Dauser S, Winter S, Eichelbaulm M, et al. CYP2D6 polymorphisms as predictors of outcome in breast cancer patients treated with tamoxifen: expanded polymorphism coverage improves risk stratification coverage. Clin Cancer Res. 2010 Jul 20.

185. Schulz C, Heinemann V, Schalhorn A, Moosmann N, Zwingers T, Boeck S, Giessen C, Stemmler HJ. UGT1A1 gene polymorphism: impact on toxicity and efficacy of irinotecan-based regimens in metastatic colorectal cancer. World J Gastroenterol. 2009 Oct 28;15(40):5058-66.

186. Schwarz UI, Ritchie MD, Bradford Y, Li C, Dudek SM, Frye-Anderson A, Kim RB, et al. Genetic determinants of response to warfarin during initial anticoagulation. N Engl J Med. 2008 Mar 6;358(10):999-1008.

187. Sconce EA, Khan TI, Wynne HA, Avery P, Monkhouse L, King BP, et al. The impact of CYP2C9 and VKORC1 genetic polymorphism and patient characteristics upon warfarin dose requirements: proposal for a new dosing regimen. Blood. 2005 Oct 1;106(7):2329-33. Epub 2005 Jun 9.

188. Scordo MG, Pengo V, Spina E, Dahl ML, Gusella M, Padrini R. Influence of CYP2C9 and CYP2C19 genetic polymorphisms on warfarin maintenance dose and metabolic clearance. Clin Pharmacol Ther. 2002 Dec;72(6):702-10.

189. Secretary's Advisory Committee on Genetic Testing. Genetics, Health and Society (SACGHS). Federal Register. Department of Health and Human Services. Rockville (MD). Available at URL address: https://www.federalregister.gov/documents/2008/04/17/E8-8216/secretarys-advisory-committee-on-genetics-health-and-society

190. Serretti A, Calati R, Massat I, Linotte S, Kasper S, Lecrubier Y, Sens-Espel R, Bollen J, Zohar J, Berlo J, Lienard P, De Ronchi D, Mendlewicz J, Souery D. Cytochrome P450 CYP1A2, CYP2C9, CYP2C19 and CYP2D6 genes are not associated with response and remission in a sample of depressive patients. Int Clin Psychopharmacol. 2009 Sep;24(5):250-6.

191. Shuldiner AR, O'Connell JR, Bliden KP, Gandhi A, Ryan K, Horenstein RB, et al. Association of cytochrome P450 2CY19 genotype with the antiplatelet effect and clinical efficacy of clopidogel therapy. JAMA. 2009 Aug 26;302(8):849-57.

192. Shulman K, Cohen I, Barnett-Griness O, Kuten A, Gruber SB, Lejbkowicz F, Rennert G. Clinical implications of UGT1A1*28 genotype testing in colorectal cancer patients. Cancer. 2011 Jul 15;117(14):3156-62. doi: 10.1002/cncr.25735.

193. Sibbing D, Koch W, Gebhard D, Schuster T, Braun S, Stegherr J, et al. Cytochrome P450 2C19*17 allelic variant, platelet aggregation, bleeding events, and stent thrombosis in clopidogrel-treated patients with coronary stent placement. Circulation. 2010 Feb 2;121(4):512-8.

194. Sibbing D, Stegherr J, Latz W, Koch W, Mehilli J, Dorrler K, et al. Cytochrome P450 2C19 loss-of-function polymorphism and stent thrombosis following percutaneous coronary intervention. Eur Heart J. 2009 Apr;30(8):916-22.

195. Siller-Matula JM, Delle-Karth G, Lang IM, Neunteufl T, Kozinski M, Kubica J, et al. Phenotyping vs genotyping for prediction of clopidogrel efficacy and safety: the PEGASUS-PCI study. J Thromb Haemost. 2012 Apr;10(4):529-42.

196. Simon T, Verstuyft C, Mary-Krause M, Quteineh L, Drouet E, Meneveneau N, et al. Genetic determinants of response to clopidogrel and cardiovascular events. N Engl J Med. 2009 Jan 22;36(4):363-75.

197. Singer DE, Albers GW, Dalen JE, Go AS, Halperin JL, Manning WJ. Antithrombotic therapy in atrial fibrillation: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):429S-56S.

198. Singh A. Pharmacogenomics--the potential of genetically guided prescribing. Aust Fam Physician. 2007 Oct;36(10):820-4.

199. Singh M, Thapa B, Arora R. Clopidogrel pharmacogenetics and its clinical implications. Am J Ther. 2010 May-Jun;17(3):e66-73.

200. Slavin TP, Niell-Swiller M, Solomon I, Nehoray B, Rybak C, Blazer KR, Weitzel JN. Clinical Application of Multigene Panels: Challenges of Next-Generation Counseling and Cancer Risk Management. Front Oncol. 2015 Sep 29;5:208.

201. Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons; Writing Committee Members, Holmes DR, Jr., Dehmer GJ, Kaul S, et al. ACCF/AHA clopidogrel clinical alert: approaches to the FDA "boxed warning" : a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the American Heart Association. Circulation. 2010 Aug 3;122(5):537-57. Epub 2010 Jun 28.

202. Sofi F, Giusti B, Marcucci R, Gori AM, Abbate R, Gensini GF. Cytochrome p450 2C19(*)2 polymorphism and cardiovascular recurrences in patients taking clopidogrel: a meta-analysis. Pharmacogenomics J. 2010 Mar 30.

203. Spina E, de Leon J. Clinical applications of CYP genotyping in psychiatry. J Neural Transm. 2015 Jan;122(1):5-28. doi: 10.1007/s00702-014-1300-5. Epub 2014 Sep 9.

204. Staatz CE, Goodman LK, Tett SE. Effect of CYP3A and ABCB1 single nucleotide polymorphisms on the pharmacokinetics and pharmacodynamics of calcineurin inhibitors: Part I. Clin Pharmacokinet. 2010 Mar;49(3):141-75.

205. Sun F, Bruening W, Uhl S, Ballard R, Tipton K, Schoelles K. Quality, regulation and clinical utility of laboratory developed molecular tests. Technology assessment report. LABC0707. Original date 2010 May 19. Correction date 2010 October 6. Accessed Nov 20, 2017. Available at URL address: http://www.cms.gov/determinationprocess/downloads/id72TA.pdf

206. Swen JJ, Huizinga TW, Gelderblom H, de Vries EG, Assendelft WJ, Kirchheiner J, et al. Translating pharmacogenomics: challenges on the road to the clinic. PLoS Med. 2007 Aug 14;4(8):e209.

207. Taguchi F, Solomon B, Gregorc V, et al. Mass Spectrometry to Classify Non-Small Cell Lung Cancer Patients for Clinical Outcome After Treatment With Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors: A Multicohort Cross Institutional Study. Journal of the National Cancer Institute, June 2007.

208. Takahashi H, Wilkinson GR, Nutescu EA, Morita T, Ritchie MD, Scordo MG, et al. Different contributions of polymorphisms in VKORC1 and CYP2C9 to intra- and inter-population differences in maintenance dose of warfarin in Japanese, Caucasians and African-Americans. Pharmacogenet Genomics. 2006 Feb;16(2):101-10.

209. Tansey KE, Guipponi M, Perroud N, Bondolfi G, Domenici E, Evans D, et al. Genetic predictors of response to serotonergic and noradrenergic antidepressants in major depressive disorder: a genome-wide analysis of individual-level data and a meta-analysis. PLoS Med. 2012;9(10):e1001326. doi: 10.1371/journal.pmed.1001326. Epub 2012 Oct 16.

210. Terasawa T, Dahabreh I, Castaldi PJ, et al. Systematic Reviews on Selected Pharmacogenetic Tests for Cancer Treatment: CYP2D6 for Tamoxifen in Breast Cancer, KRAS for anti-EGFR antibodies in Colorectal Cancer, and BCR-ABL1 for Tyrosine Kinase Inhibitors in Chronic Myeloid Leukemia [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2010 Jun 7.

211. Terrazzino S, Quaglia M, Stratta P, Canonico PL, Genazzani AA. The effect of CYP3A5 6986A>G and ABCB1 3435C>T on tacrolimus dose-adjusted trough levels and acute rejection rates in renal transplant patients: a systematic review and meta-analysis. Pharmacogenet Genomics. 2012 Aug;22 (8):642-5.

212. Thakur M, Grossman I, McCrory DC, Orlando LA, Steffens DC, Cline KE, et al. Review of evidence for genetic testing for CYP450 polymorphisms in management of patients with nonpsychotic depression with selective serotonin reuptake inhibitors. Genet Med. 2007 Dec;9(12):826-35.

213. Tham LS, Goh BC, Nafziger A, Guo JY, Wang LZ, Soong R, Lee SC. A warfarin-dosing model in Asians that uses single-nucleotide polymorphisms in vitamin K epoxide reductase complex and cytochrome P450 2C9. Clin Pharmacol Ther. 2006 Oct;80(4):346-55.

214. Trenck D, Hochholzer W, Fromm MF, Chialda LE, Pahl A, Valina CM, et al. Cytochrome P450 2C19 681G>A polymorphism and high-on clopidogrel platelet reactivity associated with adverse 1-yr clinical outcome of percutaneous coronary intervention with drug-eluting or bare-metal stents. J Am Coll Cardiol. 2008 May 20;51(20):1925-34.

215. Ulvestad M, Skottheim IB, Jakobsen GS, Bremer S, Molden E, Asberg A, et al. Impact of OATP1B1, MDR1, and CYP3A4 expression in liver and intestine on interpatient pharmacokinetic variability of atorvastatin in obese subjects. Clin Pharmacol Ther. 2013 Mar;93(3):275-82. Epub 2012 Dec 27.

216. U.S. Department of Health and Human Service. Center for Medicare and Medicaid Services. Agency for Healthcare Research and Quality; Technology Assessment: Systematic reviews on selected pharmacogenetic tests for cancer treatment: CYP2D6 for Tamoxifen in breast cancer, KRAS for anti-EGFR antibodies in colorectal cancer, and BCR-ABL1 for tyrosine kinase inhibitors in chronic myeloid leukemia. 2010 Jun 7. Accessed Nov 20, 2018. Available at URL address: https://www.cms.gov/Medicare/Coverage/DeterminationProcess/downloads/id76TA.pdf

217. U.S. Department of Health and Human Services. Center for Medicare and Medicaid Services. Agency for Healthcare Research and Quality; Technology Assessment: Testing for cytochrome p450 polymorphisms (CYP450) in adults with non-psychotic depression prior to treatment with selective serotonin reuptake inhibitors (SSRIs). No 146. Jan 2007. Accessed Nov 20, 2018. Available at URL address: https://archive.ahrq.gov/downloads/pub/evidence/pdf/cyp450/cyp450.pdf

218. U.S. Department of Health & Human Services. National Institutes of Health. Genetics Home Reference. Accessed Nov 20, 2018. Available at URL address: http://ghr.nlm.nih.gov/gene/

219. U.S. Department of Health and Human Services National Institutes of Health. National Cancer Institute (NCI). Accessed Nov 20, 2018. Available at URL address: https://www.cancer.gov/

220. U. S. Food and Drug Administration. Guidance for industry and FDA staff. Class II special controls guidance document: drug metabolizing enzyme genotyping system. Sep 12, 2013, updated Jun 24, 2014. Accessed Nov 20, 2018. Available at URL address: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077933.htm

221. U.S. Food and Drug Administration. Guidance for industry and FDA staff: Pharmacogenetic tests and genetic tests for heritable markers. 2007 June 19. Accessed Nov 20, 2018. Available at URL address: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071075.pdf

222. U.S. Food and Drug Administration. Drugs@FDA. Accessed Nov 20, 2018. Available at URL address: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

223. U.S. Food and Drug administration (FDA). Guidance for industry clinical pharmacogenomics: premarketing evaluation in early phase clinical studies and recommendations for labeling. 2013 Jan.

Accessed Nov 20, 2018. Available at URL address: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM337169.pdf

224. U.S. Food and Drug Administration. Safety Communication. The FDA Warns Against the use of Many Genetic Tests with Unapproved Claims to Predict Patient Response to Specific Medications: FDA Safety Communication. Nov 1, 2018. Accessed Nov 23, 2018. Available at URL address : https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm624725.htm?utm_campaign=The%20FDA%20Warns%20Against%20the%20use%20of%20Many%20Genetic%20Tests%20with%20Unapproved%20Claims&utm_medium=email&utm_source=Eloqua&elqTrackId=F8057CB313FF19A3460C4C37108C5851&elq=9d9bde92c7f64aa48fd86a8a2bfdee38&elqaid=5704&elqat=1&elqCampaignId=4589

225. U.S. Food and Drug Administration. Table of pharmacogenomic biomarkers in drug labels. Updated August 3, 2018. Accessed Nov 20, 2018. Available at URL address: http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm

226. U. S. Food and Drug Administration. 510(k) premarket notification. Database. metabolizing enzyme genotyping systems. Roche AmpliChip Cytochrome P450 P450 2C19- K043576. Jan 10, 2005. Accessed Nov 20, 2018. Available at URL address: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K043576

227. Vandenberghe F1, Guidi M, Choong E, von Gunten A, Conus P, Csajka C, Eap CB Genetics-Based Population Pharmacokinetics and Pharmacodynamics of Risperidone in a Psychiatric Cohort. Clin Pharmacokinet. 2015 Jul 1. [Epub ahead of print]

228. van der Bol JM, Mathijssen RH, Creemers GJ, Planting AS, Loos WJ, Wiemer EA, et al. A CYP3A4 phenotype-based dosing algorithm for individualized treatment of irinotecan. Clin Cancer Res. 2010 Jan 15;16(2):736-42.

229. Visvanathan K, Chlebowski RT, Hurley P, Col NF, Ropka M, Collyar D, et al. American Society of Clinical Oncology clinical practice guideline update on the use of pharmacologic interventions including tamoxifen, raloxifene, and aromatase inhibition for breast cancer risk reduction. J Clin Oncol. 2009 Jul 1;27(19):3235-58. Epub 2009 May 26.

230. Veenstra DL, You JH, Rieder MJ, Farin FM, Wilkerson HW, Blough DK, et al. Association of Vitamin K epoxide reductase complex 1 (VKORC1) variants with warfarin dose in a Hong Kong Chinese patient population. Pharmacogenet Genomics. 2005 Oct;15(10):687-91.

231. Vermiere S, Van Assche G, Rutgeerts P. Role of genetics in prediction of disease course and response to therapy. World J Gastroenterol. 2010 Jun 7;16(21):2609-15.

232. Visscher H, Amstutz U, Sistonen J, Ross CJ, Hayden MR, Carleton BC. Pharmacogenomics of cardiovascular drugs and adverse effects in pediatrics. J Cardiovasc Pharmacol. 2011 Sep;58(3):228-39.

233. Wadelius M, Chen LY, Eriksson N, Bumpstead S, Ghori J, Wadelius C, et al. Association of warfarin dose with genes involved in its action and metabolism. Hum Genet. 2007 Mar;121(1):23-34

234. Wadelius M, Chen LY, Downes K, Ghori J, Hunt S, Eriksson N, et al. Common VKORC1 and GGCX polymorphisms associated with warfarin dose. Pharmacogenomics J. 2005;5(4):262-70.

235. Wadelius M, Chen LY, Lindh JD, Eriksson N, Ghori MJ, Bumpstead S, et al. The largest prospective warfarin-treated cohort supports genetic forecasting. Blood. 2008 Jun 23.

236. Wang B, Canestaro WJ, Choudhry NK. Clinical evidence supporting pharmacogenomic biomarker testing provided in US Food and Drug Administration drug labels. JAMA Intern Med. 2014 Dec;174(12):1938-44.

237. Wang D, Guo Y, Wrighton SA, Cooke GE, Sadee W. Intronic polymorphism in CYP3A4 affects hepatic expression and response to statin drugs. Pharmacogenomics J. 2011 Aug;11(4):274-86.

238. Wegman P, Elingarami S, Cartensen J, Stal O, Nordenskjold B, Wingren S. Genetic variants of CYP3A5, CYP2D6, SULT1A1, UGT2B15, and tamoxifen response in postmenopausal patients with breast cancer. Breast Cancer Res. 2007;9(1):R7.

239. Winner JG, Carhart JM, Altar CA, Allen JD, Dechairo BM. A prospective, randomized, double-blind study assessing the clinical impact of integrated pharmacogenomic testing for major depressive disorder. Discov Med. 2013 Nov;16(89):219-27. Accessed Nov 30, 2018. Available at URL address: http://www.discoverymedicine.com/Joel-G-Winner/2013/11/08/a-prospective-randomized-double-blind-study-assessing-the-clinical-impact-of-integrated-pharmacogenomic-testing-for-major-depressive-disorder/

240. Xi B, Wang C, Liu L, Zeng T, Liang Y, Li J, Mi J. Association of the CYP3A5 polymorphism (6986G>A) with blood pressure and hypertension. Hypertens Res. 2011 Nov;34(11):1216-20.

241. Xu Y, Sun Y, Yao L, Shi L, Wu Y, Ouyang T, et al. Association between CYP2D6 *10 genotype and survival of breast cancer patients receiving tamoxifen treatment. Ann Oncol. 2008 Apr 11.

242. Zabalza M, Subirana I, Sala J, Lluis-Ganella C, Lucas G, Tomás M, Masiá R, Marrugat J, Brugada R, Elosua R. Meta-analyses of the association between cytochrome CYP2C19 loss- and gain-of-function polymorphisms and cardiovascular outcomes in patients with coronary artery disease treated with clopidogrel. Heart. 2012 Jan;98(2):100-8.

243. Zeir Z, Carpenter LL, Kalin, NH, McDonald WM, Widge AS, Nemeroff BB. Clinical implementation of pharmacogenetic decision support tools for antidepressant drug prescribing. Am J Pstchiatry.2Sep 1;175(9):873-886

244. Zhao W, Elie V, Roussey G, Brochard K, Niaudet P, Leroy V, et al. Population pharmacokinetics and pharmacogenetics of tacrolimus in de novo pediatric kidney transplant recipients. Clin Pharmacol Ther. 2009 Dec;86(6):609-18.

245. Zhao F, Wang J, Yang Y, Wang X, Shi R, Xu Z, Huang Z, Zhang G. Effect of CYP2C19 genetic polymorphisms on the efficacy of proton pump inhibitor-based triple therapy for Helicobacter pylori eradication: a meta-analysis. Helicobacter. 2008 Dec;13(6):532-41.

246. Zhou SF. Polymorphism of human cytochrome P450 2D6 and its clinical significance: part I. Clin Pharmacokinet. 2009;48(11):689-723.

247. Zhou SF. Polymorphism of human cytochrome P450 2D6 and its clinical significance: part II. Clin Pharmacokinet. 2009;48(12):761-804.

248. Zhu Y, Shennan M, Reynolds KK, Johnson NA, Herrnberger MR, Valdes R Jr, Linder MW. Estimation of warfarin maintenance dose based on VKORC1 (-1639 G>A) and CYP2C9 genotypes. Clin Chem. 2007 Jul;53(7):1199-205.

249. Zubenko GS, Sommer BR, Cohen BM. On the marketing and use of pharmacogenetics tests for psychiatric treatment. JAMA Psychistry. 2018 Aug 1:75(8):769-770.