Name: Jane Doe
Birth: 02.05.1988
Sex: Female
Sample ID: NA07439

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MEDICOVER GENETICS

Pharmacogenomics (PGx) Report

Medicover Pharma Passport

Gene	Genotype	Allele Functionality	Predicted phenotype
ABCG2	rs2231142 reference (G)/rs2231142 reference (G)	Normal function/Normal function	Normal Function
CYP2B6	*1/*6, *1/*38, *1/*42	Normal function/Decreased function	Intermediate Metabolizer
CYP2C19	*2/*10	No function/Decreased function	Likely Poor Metabolizer
CYP2C9	*1/*9	Normal function/Normal function	Normal Metabolizer
CYP2D6	*4/*41	No function/Decreased function	Intermediate Metabolizer
CYP3A4	*1/*1	Normal function/Normal function	Normal Metabolizer
CYP3A5	*1/*1	Normal function/Normal function	Normal Metabolizer
CYP4F2	*1/*2	Unknown/Unknown	Unknown
DPYD	Reference/Reference	Normal function/Normal function	Normal Metabolizer
G6PD	B (reference)/B (reference)	IV/Normal/IV/Normal	Normal
IFNL3	rs12979860 reference (C)/rs12979860 reference (C)	Favorable response allele/Favorable response allele	Unknown
NUDT15	*1/*1	Normal function/Normal function	Normal Metabolizer
SLCO1B1	*14/*31, *25/*31, *31/*32	Increased function/No function	Decreased Function
TPMT	*1/*1	Normal function/Normal function	Normal Metabolizer
UGT1A1	*1/*1	Normal function/Normal function	Normal Metabolizer
VKORC1	rs9923231 reference (C)/rs9923231 reference (C)	Unknown/Unknown	Unknown
ABCB1	*2/*2	high activity / high activity	high activity
ALDH2	reference/reference	normal function / normal function	normal metabolizer
BCHE	reference/reference	normal function / normal function	normal metabolizer

COMT	rs4680 variant (A)/rs4680 variant (A)	low activity / low activity	low activity
CYP1A1	reference/reference	normal function / normal function	normal metabolizer
CYP1A2	*30/*30	increased function / increased function	rapid metabolizer
CYP2C8	reference/reference	normal function / normal function	normal metabolizer
F2	reference/reference	normal function / normal function	normal metabolizer
F5	reference/reference	normal function / normal function	normal metabolizer

*Refer to the Disclaimers section regarding the interpretation of multiple allele calls

Dose Recommendations

Table 2: Dosing recommendations for drugs related to analyzed genes

Drug & Gene	Recommendations	Actionable
Drug:rosuvastatin Gene:ABCG2 Guideline:CPIC	Prescribe desired starting dose and adjust doses of rosuvastatin based on disease-specific and specific population guidelines. Prescriber should be aware of possible increased risk for myopathy especially for doses gt;20mg.The potential for drug-drug interactions and dose limits based on renal and hepatic function and Asian ancestry should be evaluated prior to initiating a statin. The effects of drug-drug interactions may be more pronounced resulting in a higher risk of myopathy. (**PMID**: *35152405*)	Yes
Drug:efavirenz Gene:CYP2B6 Guideline:CPIC	Consider initiating efavirenz with decreased dose of 400 mg/dayIf therapeutic drug monitoring is available and a decreased efavirenz dose is prescribed, consider obtaining steady-state plasma efavirenz concentrations to ensure concentrations are in the suggested therapeutic range (~1 to 4 g/mL). To prescribe efavirenz at a decreased dose of 400 mg/day or 200 mg/day in a multidrug regimen may require prescribing more than one pill once daily. If so, the provider should weigh the potential benefit of reduced dose against the potential detrimental impact of increased pill number. (**PMID**: *31006110*)	Yes
Drug:sertraline Gene:CYP2B6 Guideline:CPIC	Consider a lower starting dose, slower titration schedule and 50% reduction of standard maintenance dose as compared to CYP2C19 normal metabolizers or select a clinically appropriate alternative antidepressant not predominantly metabolized by CYP2C19. (**PMID**: *25974703*, *37032427*)	Yes
Drug:abrocitinib Gene:CYP2C19 Guideline:FDA	Results in higher systemic concentrations and may result in higher adverse reaction risk. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations. (**PMID**: *None*)	Yes
Drug:amitriptyline Gene:CYP2C19 Guideline:CPIC	Avoid amitriptyline use; If amitriptyline is warranted, utilize therapeutic drug monitoring to guide dose adjustment. Utilizing therapeutic drug monitoring to guide dose adjustments is strongly recommended.Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendationsfor conditions where lower initial doses are used, such as neuropathic pain. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Utilizing therapeutic drug monitoring if a tricyclic is prescribed to a patient with CYP2D6 ultrarapid, intermediate or poor metabolism in combination with CYP2C19 ultrarapid, intermediate or poor metabolism is strongly recommended. (**PMID**: *23486447*, *27997040*)	Yes
Drug:belzutifan Gene:CYP2C19 Guideline:FDA	Results in higher systemic concentrations and may result in higher adverse reaction risk (anemia, hypoxia). Monitor patients who are poor metabolizers for both genes for adverse reactions. (**PMID**: *None*)	Yes
Drug:brivaracetam Gene:CYP2C19 Guideline:FDA	Results in higher systemic concentrations and higher adverse reaction risk. Consider dosage reductions in poor metabolizers. (**PMID**: *None*)	Yes
Drug:carisoprodol Gene:CYP2C19 Guideline:FDA	Results in higher systemic concentrations. Use with caution. (**PMID**: *None*)	Yes

Drug:citalopram Gene:CYP2C19 Guideline:CPIC	Consider a clinically appropriate antidepressant not predominantly metabolized by CYP2C19. If citalopram or escitalopram are clinically appropriate, consider a lower starting dose, slower titration schedule and 50% reduction of the standard maintenance dose as compared to normal metabolizers.Per the FDA warning, citalopram 20 mg/day is the maximum recommended dose in CYP2C19 poor metabolizers due to the risk of QT prolongation. FDA product labeling additionally cautions that citalopram dose should be limited to 20 mg/day in patients with hepatic impairment, those taking a CYP2C19 inhibitor, and patients greater than 60 years of age. (**PMID**: *25974703*, *37032427*)	Yes
Drug:clobazam Gene:CYP2C19 Guideline:FDA	Results in higher systemic active metabolite concentrations. Poor metabolism results in higher adverse reaction risk. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations. (**PMID**: *None*)	Yes
Drug:clomipramine Gene:CYP2C19 Guideline:CPIC	Avoid clomipramine use; If clomipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment. Utilizing therapeutic drug monitoring to guide dose adjustments is strongly recommended.Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendationsfor conditions where lower initial doses are used, such as neuropathic pain. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Utilizing therapeutic drug monitoring if a tricyclic is prescribed to a patient with CYP2D6 ultrarapid, intermediate or poor metabolism in combination with CYP2C19 ultrarapid, intermediate or poor metabolism is strongly recommended. (**PMID**: *23486447*, *27997040*)	Yes
Drug:clopidogrel Gene:CYP2C19 Guideline:CPIC	Avoid clopidogrel if possible. Use prasugrel or ticagrelor at standard dose if no contraindication.For cardiovascular indications of acute coronary syndrome (ACS) and/or percutaneous coronary intervention (PCI). ACS and/or PCI includes patients undergoing PCI for an ACS or non-ACS (elective) indication. The strength of recommendation for likely phenotypes are the same as their respective confirmed phenotypes. Likely indicates the uncertainty in the phenotype assignment, but it is reasonable to apply the recommendation for the confirmed phenotype to the corresponding likely phenotype. (**PMID**: *21716271*, *23698643*, *35034351*)	Yes
Drug:dexlansoprazole Gene:CYP2C19 Guideline:CPIC	Initiate standard starting daily dose. For chronic therapy (gt;12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.The strength of recommendation for likely phenotypes are the same as their respective confirmed phenotypes. Likely indicates the uncertainty in the phenotype assignment, but it is reasonable to apply the recommendation for the confirmed phenotype to the corresponding likely phenotype. (**PMID**: *32770672*)	Yes
Drug:diazepam Gene:CYP2C19 Guideline:FDA	May affect systemic concentrations. (**PMID**: *None*)	Yes

Drug:doxepin Gene:CYP2C19 Guideline:CPIC	Avoid doxepin use; If doxepin is warranted, utilize therapeutic drug monitoring to guide dose adjustment. Utilizing therapeutic drug monitoring to guide dose adjustments is strongly recommended.Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendationsfor conditions where lower initial doses are used, such as neuropathic pain. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Utilizing therapeutic drug monitoring if a tricyclic is prescribed to a patient with CYP2D6 ultrarapid, intermediate or poor metabolism in combination with CYP2C19 ultrarapid, intermediate or poor metabolism is strongly recommended. (**PMID**: *23486447*, *27997040*)	Yes
Drug:escitalopram Gene:CYP2C19 Guideline:CPIC	Consider a clinically appropriate antidepressant not predominantly metabolized by CYP2C19. If citalopram or escitalopram are clinically appropriate, consider a lower starting dose, slower titration schedule and 50% reduction of the standard maintenance dose as compared to normal metabolizers.Per the FDA warning, citalopram 20 mg/day is the maximum recommended dose in CYP2C19 poor metabolizers due to the risk of QT prolongation. FDA product labeling additionally cautions that citalopram dose should be limited to 20 mg/day in patients with hepatic impairment, those taking a CYP2C19 inhibitor, and patients greater than 60 years of age. (**PMID**: *25974703*, *37032427*)	Yes
Drug:esomeprazole Gene:CYP2C19 Guideline:FDA	Results in higher systemic concentrations. (**PMID**: *None*)	Yes
Drug:flibanserin Gene:CYP2C19 Guideline:FDA	May result in higher systemic concentrations and higher adverse reaction risk. Monitor patients for adverse reactions. (**PMID**: *None*)	Yes
Drug:imipramine Gene:CYP2C19 Guideline:CPIC	Avoid imipramine use; If imipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment. Utilizing therapeutic drug monitoring to guide dose adjustments is strongly recommended.Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendationsfor conditions where lower initial doses are used, such as neuropathic pain. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Utilizing therapeutic drug monitoring if a tricyclic is prescribed to a patient with CYP2D6 ultrarapid, intermediate or poor metabolism in combination with CYP2C19 ultrarapid, intermediate or poor metabolism is strongly recommended. (**PMID**: *23486447*, *27997040*)	Yes
Drug:lansoprazole Gene:CYP2C19 Guideline:CPIC	Initiate standard starting daily dose. For chronic therapy (gt;12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.The strength of recommendation for likely phenotypes are the same as their respective confirmed phenotypes. Likely indicates the uncertainty in the phenotype assignment, but it is reasonable to apply the recommendation for the confirmed phenotype to the corresponding likely phenotype. (**PMID**: *32770672*)	Yes
Drug:mavacamten Gene:CYP2C19 Guideline:FDA	Results in higher systemic concentrations and may have higher adverse reaction risk (heart failure). Dosage is based on individual response. The dose titration and monitoring schedule accounts for differences due to CYP2C19 genetic variation, so adjustments based on CYP2C19 genotype are not necessary. Refer to FDA labeling for specific dosing recommendations and monitoring. (**PMID**: *None*)	Yes

Drug:omeprazole Gene:CYP2C19 Guideline:CPIC	Initiate standard starting daily dose. For chronic therapy (gt;12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.The strength of recommendation for likely phenotypes are the same as their respective confirmed phenotypes. Likely indicates the uncertainty in the phenotype assignment, but it is reasonable to apply the recommendation for the confirmed phenotype to the corresponding likely phenotype. (**PMID**: *32770672*)	Yes
Drug:pantoprazole Gene:CYP2C19 Guideline:CPIC	Initiate standard starting daily dose. For chronic therapy (gt;12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.The strength of recommendation for likely phenotypes are the same as their respective confirmed phenotypes. Likely indicates the uncertainty in the phenotype assignment, but it is reasonable to apply the recommendation for the confirmed phenotype to the corresponding likely phenotype. (**PMID**: *32770672*)	Yes
Drug:rabeprazole Gene:CYP2C19 Guideline:FDA	Results in higher systemic concentrations. (**PMID**: *None*)	Yes
Drug:trimipramine Gene:CYP2C19 Guideline:CPIC	Avoid trimipramine use; If trimipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment. Utilizing therapeutic drug monitoring to guide dose adjustments is strongly recommended.Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendationsfor conditions where lower initial doses are used, such as neuropathic pain. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Utilizing therapeutic drug monitoring if a tricyclic is prescribed to a patient with CYP2D6 ultrarapid, intermediate or poor metabolism in combination with CYP2C19 ultrarapid, intermediate or poor metabolism is strongly recommended. (**PMID**: *23486447*, *27997040*)	Yes
Drug:voriconazole Gene:CYP2C19 Guideline:CPIC	Choose an alternative agent that is not dependent on CYP2C19 metabolism as primary therapy in lieu of voriconazole. Such agents include isavuconazole, liposomal amphotericin B, and posaconazole. In the event that voriconazole is considered to be the most appropriate agent, based on clinical advice, for a patient with poor metabolizer genotype, voriconazole should be administered at a preferably lower than standard dosage with careful therapeutic drug monitoring.Further dose adjustments or selection of alternative therapy may be necessary due to other clinical factors, such as drug interactions, hepatic function, renal function, species, site of infection, therapeutic drug monitoring, and comorbidities. (**PMID**: *27981572*)	Yes
Drug:celecoxib Gene:CYP2C9 Guideline:CPIC	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. (**PMID**: *32189324*)	No
Drug:flurbiprofen Gene:CYP2C9 Guideline:CPIC	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. (**PMID**: *32189324*)	No
Drug:fluvastatin Gene:CYP2C9 Guideline:CPIC	Prescribe desired starting dose and adjust doses of fluvastatin based on disease-specific guidelines. Prescriber should be aware of possible increased risk for myopathy especially for doses gt;40mg per day.The potential for drug-drug interactions and dose limits based on renal and hepatic function should be evaluated prior to initiating a statin. The effects of drug-drug interactions may be more pronounced resulting in a higher risk of myopathy. (**PMID**: *35152405*)	Yes

Drug:fosphenytoin Gene:CYP2C9 Guideline:CPIC	No adjustments needed from typical dosing strategies. Subsequent doses should be adjusted according to therapeutic drug monitoring, response, and side effects. An HLA-B*15:02 negative test does not eliminate the risk of phenytoin-induced SJS/TEN and patients should be carefully monitored according to a usual standard. (**PMID**: *25099164*, *32779747*)	No
Drug:ibuprofen Gene:CYP2C9 Guideline:CPIC	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. (**PMID**: *32189324*)	No
Drug:lornoxicam Gene:CYP2C9 Guideline:CPIC	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. (**PMID**: *32189324*)	No
Drug:meloxicam Gene:CYP2C9 Guideline:CPIC	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. (**PMID**: *32189324*)	No
Drug:phenytoin Gene:CYP2C9 Guideline:CPIC	No adjustments needed from typical dosing strategies. Subsequent doses should be adjusted according to therapeutic drug monitoring, response, and side effects. An HLA-B*15:02 negative test does not eliminate the risk of phenytoin-induced SJS/TEN and patients should be carefully monitored according to a usual standard. (**PMID**: *25099164*, *32779747*)	No
Drug:piroxicam Gene:CYP2C9 Guideline:CPIC	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. (**PMID**: *32189324*)	No
Drug:tenoxicam Gene:CYP2C9 Guideline:CPIC	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. (**PMID**: *32189324*)	No
Drug:warfarin Gene:CYP2C9 Guideline:CPIC	Unknown (**PMID**: *21900891*, *28198005*)	No
Drug:amitriptyline Gene:CYP2D6 Guideline:FDA	May alter systemic concentrations. (**PMID**: *None*)	Yes
Drug:amoxapine Gene:CYP2D6 Guideline:FDA	May alter systemic concentrations. (**PMID**: *None*)	Yes
Drug:atomoxetine Gene:CYP2D6 Guideline:CPIC	Initiate with a dose of 40 mg/day and if no clinical response and in the absence of adverse events after 2 weeks increase dose to 80 mg/day. If response is inadequate after 2 weeks consider obtaining a plasma concentration 2-4 h after dosing. If concentration is lt;200 ng/mL, consider a proportional dose increase to achieve a concentration to approach 400 ng/mL. If unacceptable side effects are present at any time, consider a reduction in dose.Therapeutic range of 200 to 1000 ng/mL has been proposed (PMID 29493375). Limited data are available regarding the relationship between atomoxetine plasma concentrations and clinical response. Available information suggests that clinical response is greater in poor metabolizers (PMs) compared to non-PMs and may be related to the higher plasma concentrations 1 to 1.5 hours after dosing in PMs compared to non-PMs administered a similar dose. Furthermore, modest improvement in response, defined as reduction in ADHD-rating scale, is observed at peak concentrations greater than 400 ng/mL. (**PMID**: *30801677*)	Yes
Drug:clomipramine Gene:CYP2D6 Guideline:FDA	May alter systemic concentrations. (**PMID**: *None*)	Yes

Drug:codeine Gene:CYP2D6 Guideline:CPIC	Use codeine label recommended age- or weight-specific dosing. If no response and opioid use is warranted, consider a non-tramadol opioid. (**PMID**: *22205192*, *24458010*, *33387367*)	Yes
Drug:desipramine Gene:CYP2D6 Guideline:CPIC	Consider a 25% reduction of recommended starting dose. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Utilize therapeutic drug monitoring to guide dose adjustments.Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendations for conditions where lower initial doses are used, such as neuropathic pain. (**PMID**: *23486447*, *27997040*)	Yes
Drug:deutetrabenazi Gene:CYP2D6 Guideline:FDA	Results in higher systemic concentrations and adverse reaction risk (QT prolongation). The maximum recommended dosage should not exceed 36 mg (maximum single dose of 18 mg). (**PMID**: *None*)	Yes
Drug:eliglustat Gene:CYP2D6 Guideline:FDA	Alters systemic concentrations, effectiveness, and adverse reaction risk (QT prolongation). Indicated for normal, intermediate, and poor metabolizer patients. Ultrarapid metabolizers may not achieve adequate concentrations to achieve a therapeutic effect. The recommended dosages are based on CYP2D6 metabolizer status. Coadministration with strong CYP3A inhibitors is contraindicated in intermediate and poor CYP2D6 metabolizers. Refer to FDA labeling for specific dosing recommendations. (**PMID**: *None*)	Yes
Drug:fluvoxamine Gene:CYP2D6 Guideline:CPIC	Initiate therapy with recommended starting dose. (**PMID**: *25974703*, *37032427*)	No
Drug:hydrocodone Gene:CYP2D6 Guideline:CPIC	Use hydrocodone label recommended age- or weight-specific dosing. If no response and opioid use is warranted, consider non-codeine or non-tramadol opioid. (**PMID**: *33387367*)	Yes
Drug:imipramine Gene:CYP2D6 Guideline:FDA	May alter systemic concentrations. (**PMID**: *None*)	Yes
Drug:meclizine Gene:CYP2D6 Guideline:FDA	May affect systemic concentrations. Monitor for adverse reactions and clinical effect. (**PMID**: *None*)	Yes
Drug:nortriptyline Gene:CYP2D6 Guideline:CPIC	Consider a 25% reduction of recommended starting dose. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Utilize therapeutic drug monitoring to guide dose adjustments.Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Dosing recommendations only apply to higher initial doses of tricyclic antidepressants for treatment of conditions such as depression. See other considerations for dosing recommendations for conditions where lower initial doses are used, such as neuropathic pain. (**PMID**: *23486447*, *27997040*)	Yes
Drug:ondansetron Gene:CYP2D6 Guideline:CPIC	Insufficient evidence demonstrating clinical impact based on CYP2D6 genotype. Initiate therapy with recommended starting dose.Drug-drug interactions and other patient characteristics (e.g., age, renal function, and liver function) should be considered when selecting alternative therapy. (**PMID**: *28002639*)	No
Drug:paroxetine Gene:CYP2D6 Guideline:CPIC	Consider a lower starting dose and slower titration schedule as compared to normal metabolizers.Drug-drug interactions and other patient characteristics (e.g., age, renal function, liver function) should be considered when adjusting dose or selecting an alternative therapy. (**PMID**: *25974703*, *37032427*)	Yes

Drug:tamoxifen Gene:CYP2D6 Guideline:CPIC	Consider hormonal therapy such as an aromatase inhibitor for postmenopausal women or aromatase inhibitor along with ovarian function suppression in premenopausal women, given that these approaches are superior to tamoxifen regardless of CYP2D6 genotype (PMID 26211827). If aromatase inhibitor use is contraindicated, consideration should be given to use a higher but FDA approved tamoxifen dose (40 mg/day)(PMID 27226358). Avoid CYP2D6 strong to weak inhibitors. (**PMID**: *29385237*)	Yes
Drug:tramadol Gene:CYP2D6 Guideline:CPIC	Use tramadol label recommended age- or weight-specific dosing. If no response and opioid use is warranted, consider non-codeine opioid. (**PMID**: *33387367*)	Yes
Drug:trimipramine Gene:CYP2D6 Guideline:FDA	May alter systemic concentrations. (**PMID**: *None*)	Yes
Drug:tropisetron Gene:CYP2D6 Guideline:CPIC	Insufficient evidence demonstrating clinical impact based on CYP2D6 genotype. Initiate therapy with recommended starting dose.Drug-drug interactions and other patient characteristics (e.g., age, renal function, and liver function) should be considered when selecting alternative therapy. (**PMID**: *28002639*)	No
Drug:venlafaxine Gene:CYP2D6 Guideline:CPIC	No action recommended based on genotype for venlafaxine because of minimal evidence regarding the impact on efficacy or side effects. (**PMID**: *37032427*)	No
Drug:vortioxetine Gene:CYP2D6 Guideline:CPIC	Initiate therapy with recommended starting dose. (**PMID**: *37032427*)	No
Drug:tacrolimus Gene:CYP3A5 Guideline:CPIC	Increase starting dose 1.5 to 2 times recommended starting dose. Total starting dose should not exceed 0.3 mg/kg/day. Use therapeutic drug monitoring to guide dose adjustments.This recommendation includes the use of tacrolimus in kidney, heart, lung and hematopoietic stem cell transplant patients, and liver transplant patients where the donor and recipient genotypes are identical. Further dose adjustments or selection of alternative therapy may be necessary due to other clinical factors (e.g., medication interactions, or hepatic function). Typically with other CYP enzymes, a normal metabolizer would be classified as having normal metabolism, and therefore, the drug dose would not change based on the patient's genotype. However, in the case of CYP3A5 and tacrolimus, a CYP3A5 expresser (i.e., CYP3A5 normal metabolizer or intermediate metabolizer) would require a higher recommended starting dose, and the CYP3A5 non-expresser (i.e., poor metabolizer) would require the standard recommended starting dose. (**PMID**: *25801146*)	Yes
Drug:capecitabine Gene:DPYD Guideline:CPIC	Based on genotype, there is no indication to change dose or therapy. Use label-recommended dosage and administration. (**PMID**: *23988873*, *29152729*)	No
Drug:fluorouracil Gene:DPYD Guideline:CPIC	Based on genotype, there is no indication to change dose or therapy. Use label-recommended dosage and administration. (**PMID**: *23988873*, *29152729*)	No
Drug:dapsone Gene:G6PD Guideline:CPIC	No reason to avoid based on G6PD status (**PMID**: *24787449*, *36049896*)	No
Drug:methylene blue Gene:G6PD Guideline:CPIC	No reason to avoid based on G6PD status (**PMID**: *24787449*, *36049896*)	No
Drug:nitrofurantoin Gene:G6PD Guideline:CPIC	No reason to avoid based on G6PD status ( )	No

Drug:pegloticase Gene:G6PD Guideline:CPIC	No reason to avoid based on G6PD status (**PMID**: *24787449*, *36049896*)	No
Drug:primaquine Gene:G6PD Guideline:CPIC	No reason to avoid based on G6PD status (**PMID**: *36049896*)	No
Drug:rasburicase Gene:G6PD Guideline:CPIC	No reason to avoid based on G6PD status (**PMID**: *24787449*, *36049896*)	No
Drug:tafenoquine Gene:G6PD Guideline:CPIC	No reason to avoid based on G6PD statusTafenoquine's safety has been established for a G6PD enzyme activity 70% of normal. (Inclusion criteria for clinical trials involving tafenoquine included G6PD activity 70%.) (**PMID**: *24787449*, *36049896*)	No
Drug:toluidine blue Gene:G6PD Guideline:CPIC	No reason to avoid based on G6PD statusToluidine blue classification strength is based on extrapolation from methylene blue data (**PMID**: *24787449*, *36049896*)	No
Drug:azathioprine Gene:NUDT15 Guideline:CPIC	Start with normal starting dose (e.g., 2-3 mg/kg/day) and adjust doses of azathioprine based on disease-specific guidelines. Allow 2 weeks to reach steady-state after each dose adjustment (PMID 20354201, 11302950, 15606506).Normal starting doses vary by race/ethnicity and treatment regimens. If standard dose is below normal recommended dose, dose reduction might not be recommended for intermediate metabolizers. (**PMID**: *21270794*, *23422873*, *30447069*)	No
Drug:mercaptopurine Gene:NUDT15 Guideline:CPIC	Start with normal starting dose (e.g., 75 mg/m2/day or 1.5 mg/kg/day) and adjust doses of mercaptopurine (and of any other myelosuppressive therapy) without any special emphasis on mercaptopurine compared to other agents. Allow at least 2 weeks to reach steady-state after each dose adjustment (PMID 20354201, 16401827, 11302950).Normal starting doses vary by race/ethnicity and treatment regimens. If standard dose is below normal recommended dose, dose reduction might not be recommended for intermediate metabolizers. (**PMID**: *21270794*, *23422873*, *30447069*)	No
Drug:thioguanine Gene:NUDT15 Guideline:CPIC	Start with normal starting dose (e.g., 40-60 mg/m2/day) and adjust doses of thioguanine and of other myelosuppressive therapy without any special emphasis on thioguanine. Allow 2 weeks to reach steady-state after each dose adjustment (PMID 20354201, 11037857).Normal starting doses vary by race/ethnicity and treatment regimens. If standard dose is below normal recommended dose, dose reduction might not be recommended for intermediate metabolizers. (**PMID**: *21270794*, *23422873*, *30447069*)	No
Drug:atorvastatin Gene:SLCO1B1 Guideline:CPIC	Prescribe $\leq$40mg as a starting dose and adjust doses of atorvastatin based on disease-specific guidelines. Prescriber should be aware of possible increased risk for myopathy especially for 40mg dose. If dose gt;40mg needed for desired efficacy, consider combination therapy (i.e., atorvastatin plus non-statin guideline directed medical therapy) (PMID: 30423391).The potential for drug-drug interactions and dose limits based on renal and hepatic function should be evaluated prior to initiating a statin. The effects of drug-drug interactions may be more pronounced resulting in a higher risk of myopathy. (**PMID**: *35152405*)	Yes
Drug:lovastatin Gene:SLCO1B1 Guideline:CPIC	Prescribe an alternative statin depending on the desired potency (see Figure 1 of PMID: 35152405 for recommendations for alternative statins). If lovastatin therapy is warranted, limit dose to $\leq$20mg/day.The potential for drug-drug interactions and dose limits based on renal and hepatic function should be evaluated prior to initiating a statin. The effects of drug-drug interactions may be more pronounced resulting in a higher risk of myopathy. (**PMID**: *35152405*)	Yes

Drug:pitavastatin Gene:SLCO1B1 Guideline:CPIC	Prescribe $\leq$ 2mg as a starting dose and adjust doses of pitavastatin based on disease-specific guidelines. Prescriber should be aware of possible increased risk for myopathy especially for doses gt;1mg. If dose gt;2mg needed for desired efficacy, consider an alternative statin (see Figure 1 of PMID: 35152405 for recommendations for alternative statins) or combination therapy (i.e. pitavastatin plus non-statin guideline directed medical therapy) (PMID: 30423391).The potential for drug-drug interactions and dose limits based on renal and hepatic function should be evaluated prior to initiating a statin. The effects of drug-drug interactions may be more pronounced resulting in a higher risk of myopathy. (**PMID**: *35152405*)	Yes
Drug:pravastatin Gene:SLCO1B1 Guideline:CPIC	Prescribe desired starting dose and adjust doses of pravastatin based on disease-specific guidelines. Prescriber should be aware of possible increased risk for myopathy with pravastatin especially with doses gt;40mg per day.The potential for drug-drug interactions and dose limits based on renal and hepatic function should be evaluated prior to initiating a statin. The effects of drug-drug interactions may be more pronounced resulting in a higher risk of myopathy. (**PMID**: *35152405*)	Yes
Drug:simvastatin Gene:SLCO1B1 Guideline:CPIC	Prescribe an alternative statin depending on the desired potency (see Figure 1 of PMID: 35152405 for recommendations for alternative statins). If simvastatin therapy is warranted, limit dose to lt;20mg/day.The potential for drug-drug interactions and dose limits based on renal and hepatic function should be evaluated prior to initiating a statin. The effects of drug-drug interactions may be more pronounced resulting in a higher risk of myopathy. (**PMID**: *22617227*, *24918167*, *35152405*)	Yes
Drug:atazanavir Gene:UGT1A1 Guideline:CPIC	There is no need to avoid prescribing of atazanavir based on UGT1A1 genetic test result. Inform the patient that some patients stop atazanavir because of jaundice (yellow eyes and skin), but that this patient's genotype makes this unlikely (less than about a 1 in 20 chance of stopping atazanavir because of jaundice).All studies correlating UGT1A1 genotypes with atazanavir adverse events have involved ritonavir boosting. However, concentration-time profiles are equivalent when boosted with either cobicistat or ritonavir (PMID 23532097), and bilirubin-related adverse events including discontinuation of atazanavir occur in a similar percentage of patients prescribed atazanavir with cobicistat or ritonavir (PMID 23532097). Associations between UGT1A1 genotype, bilirubin elevations, and atazanavir/r discontinuation therefore almost certainly translate to atazanavir/cobicistat. reference function refers to the UGT1A1 allele to which other alleles are compared. (**PMID**: *26417955*)	Yes

Analyzed Genes and Variants

Table 3: List of genes and loci evaluated in this assay together with haplotypes that can be called

Gene	Analyzed rsIDs	Analyzed haplotypes
ABCB1	rs1045642	*2
ABCG2	rs2231142, rs72552713	*S1
ALDH2	rs671	111803962:G>A
BCHE	rs1803274, rs1799807	K-Variant, A-Variant
COMT	rs4680	19963748:G>A
CYP1A1	rs1800031, rs41279188, rs1048943, rs1799814, rs72547509, rs72547510, rs56313657	*2,*3,*4,*5,*6,*7,*8,*9,
CYP1A2	rs56107638, rs762551	*7, *30
CYP2B6	rs34223104, rs34883432, rs8192709, rs33973337, rs33980385, rs33926104, rs34284776, rs35303484, rs139801276, rs12721655, rs535039125, rs35773040, rs145884402, rs3826711, rs36056539, rs3745274, rs58871670, rs373489637, rs45482602, rs2279343, rs28399499, rs34826503, rs754621576, rs780991919, rs34097093, rs200458614, rs201500445, rs200238771, rs117872433, rs564083989, rs3211371	*1, *2, *4, *6, *7, *8, *9, *10, *13, *18, *19, *20, *26, *28, *34, *36, *37, *38, *39, *40, *41, *42, *43
CYP2C8	rs10509681, rs11572103, rs1058930, rs72558195, rs72558196, rs11572080	*2, *3, *4, *5, *7, *8
CYP2C9	rs114071557, rs67807361, rs142240658, rs1364419386, rs2031308986, rs371055887, rs72558187, rs762239445, rs1304490498, rs774607211, rs72558188, rs767576260, rs12414460, rs375805362, rs72558189, rs1375956433, rs200965026, rs199523631, rs200183364, rs1799853, rs141489852, rs754487195, rs1289704600, rs17847037, rs7900194, rs72558190, rs774550549, rs2256871, rs9332130, rs9332131, rs72558192, rs988617574, rs1237225311, rs57505750, rs28371685, rs367826293, rs1274535931, rs750820937, rs1297714792, rs749060448, rs1057910, rs56165452, rs28371686, rs1250577724, rs578144976, rs767284820, rs781583846, rs9332239, rs868182778	*1, *2, *3, *4, *5, *6, *8, *9, *10, *11, *12, *13, *15, *18, *27, *35, *61, *68, *71
CYP2C19	rs12248560, rs28399504, rs367543002, rs367543003, rs55752064, rs17882687, rs1564656981, rs145328984, rs1564660997, rs118203756, rs1288601658, rs41291556, rs17885179, rs72552267, rs17884712, rs58973490, rs140278421, rs370803989, rs4986893, rs6413438, rs4244285, rs375781227, rs72558186, rs138142612, rs3758581, rs118203757, rs56337013, rs192154563, rs118203759, rs55640102	*1, *2, *3, *4, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14, *15, *17, *18, *19, *22, *23, *24, *25, *26, *28, *29, *31, *32, *33, *35, *38, *39

CYP2D6	whole gene (exons + introns)	*1, *1xN, *2, *2xN, *3, *3xN, *4, *4xN, *5, *6, *6xN, *7, *8, *9, *9xN, *10, *10xN, *11, *12, *13, *14, *15, *17, *17xN, *18, *19, *20, *21, *22, *23, *24, *25, *26, *27, *28, *29, *29xN, *30, *31, *32, *33, *34, *35, *35xN, *36, *36xN, *37, *38, *39, *40, *41, *41xN, *42, *43, *43xN, *44, *45, *45xN, *46, *47, *48, *49, *50, *51, *52, *53, *54, *55, *56, *58, *59, *60, *61, *62, *63, *64, *65, *68, *69, *70, *71, *72, *73, *74, *75, *81, *82, *83, *84, *85, *86, *87, *88, *89, *90, *91, *92, *93, *94, *95, *96, *97, *98, *99, *100, *101, *102, *103, *104, *105, *106, *107, *108, *109, *110, *111, *112, *113, *114, *115, *116, *117, *118, *119, *120, *121, *122, *123, *124, *125, *126, *127, *128, *129, *130, *131, *132, *133, *134, *135, *136, *137, *138, *139, *140, *141, *142, *143, *144, *145, *146, *146x2, *147, *148, *149, *152, *153, *154, *155, *156, *157, *158, *159, *160, *161, *162, *163
CYP3A4	rs67666821, rs4986913, rs4986910, rs774109750, rs4986909, rs12721629, rs756833413, rs67784355, rs4646438, rs138105638, rs55785340, rs55901263, rs113667357, rs4987161, rs12721627, rs35599367, rs4986908, rs72552798, rs4986907, rs57409622	*2, *6, *20, *22
CYP3A5	rs41279854, rs41303343, rs28383479, rs10264272, rs55965422, rs776746, rs55817950	*1, *3, *6, *7
CYP4F2	rs2108622, rs114099324, rs3093105	*1, *2, *3, *4, *17
DPYD	rs114096998, rs148799944, rs140114515, rs1801268, rs139459586, rs202144771, rs72547601, rs72547602, rs145529148, rs141044036, rs67376798, rs1801267, rs147545709, rs55674432, rs201035051, rs3918290, rs3918289, rs72549303, rs17376848, rs186169810, rs142512579, rs764666241, rs200064537, rs56038477, rs61622928, rs143815742, rs140602333, rs78060119, rs75017182, rs1801266, rs150385342, rs72549309, rs1801265, rs80081766, rs72549310	*S10, *S9, *S11, *S12, *S3, *S3, *S16, *S17
F2	rs1799963	46739505:G>A
F5	rs6025	169549811:C>T

G6PD	rs137852348, rs137852344, rs72554664, rs782608284, rs72554665, rs137852324, rs398123546, rs137852317, rs137852337, rs782098548, rs137852336, rs137852323, rs137852325, rs137852335, rs137852316, rs137852321, rs137852334, rs137852320, rs137852322, rs371489738, rs137852329, rs137852345, rs137852333, rs34193178, rs398123544, rs137852342, rs5030869, rs76723693, rs137852347, rs137852339, rs137852327, rs74575103, rs137852318, rs137852346, rs782757170, rs137852328, rs137852319, rs137852326, rs782754619, rs781865768, rs137852332, rs137852330, rs5030868, rs267606836, rs5030872, rs137852343, rs137852331, rs137852314, rs370918918, rs782487723, rs137852313, rs782322505, rs78365220, rs1050829, rs5030870, rs267606835, rs181277621, rs782308266, rs138687036, rs782090947, rs137852349, rs1050828, rs137852315, rs76645461, rs78478128, rs137852338, rs137852340	B
IFNL3	rs12979860	39248147C>T
NUDT15	48037782:AGGAGTC>AGGAGTCGGAGTC, 48045719:C>T, 48045720:G>A, 48037798:G>A, 48037847:G>C, 48037849:A>G, 48037782:AGGAGTC>A, 48037748:T>C, 48037885:G>A, 48037902:C>G, 48041103:T>TG, 48037825:C>CGCGG, 48045771:T>A, 48037834:C>T, 48041113:G>T, 48040977:GA>G, 48037749:G>C, 48045690:C>G	*1, *2, *3, *4, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14, *15, *16, *17, *18, *19, *20
SLCO1B1	rs139257324, rs373327528, rs56101265, rs56061388, rs2306283, rs2306282, rs11045819, rs72559745, rs77271279, rs141467543, rs4149056, rs55901008, rs59502379, rs74064213, rs34671512, rs56199088, rs55737008, rs200995543, rs140790673	*1, *2, *3, *4, *5, *6, *9, *10, *11, *12, *13, *14, *15, *20, *24, *25, *27, *28, *29, *30, *31, *32, *33, *37, *39, *40, *42, *43, *44, *46, *47
TPMT	rs1142345, rs150900439, rs72552736, rs139392616, rs398122996, rs56161402, rs377085266, rs1800584, rs144041067, rs112339338, rs1800460, rs72552737, rs111901354, rs1800462, rs1256618794	*1, *2, *3A, *3B, *3C, *4, *8, *41
UGT1A1	rs4124874, rs4148323, rs35350960, rs55750087, rs3499378	*1, *6, *27
VKORC1	rs7294, rs9934438, rs17708472, rs9923231	-1639 AA, -1639 AG, -1639 GG

Description of genes analyzed in this study

Table 4: Description of all analyzed genes

Gene	Description
CYP2D6	The enzyme CYP2D6 is involved in the metabolism of 20-30% of commonly prescribed drugs. Pathogenic alterations in the CYP2D6 gene can lead to different metabolizer types that influence drug response, with the "slow metabolizer type" occurring in 7% and the "intermediate type" in 40% of the Caucasian population. The "ultra-rapid metabolizer type" shows increased enzyme activity. Dose adjustments based on the metabolizer type can reduce side effects and increase treatment efficacy.
CYP2B6	The enzyme CYP2B6 is involved in the metabolism of various drugs. The CYP2B6*4 allele is associated with increased enzyme activity. Various other alleles lead to reduced activity. Dose adjustments based on the metabolizer type can reduce side effects and resistance to therapy.
CYP2C9	The enzyme CYP2C9 is involved in the metabolism of various drugs. Variants in the CYP2C9 gene lead to reduced enzyme activity and poor or intermediate metabolizer phenotype. Dose adjustments based on the metabolizer type can reduce side effects.
CYP3A5	The enzyme CYP3A5 is involved in the metabolism of various drugs. Most Caucasians carry the CYP3A4*3/*3 genotype, which is associated with the so-called non-expressor phenotype and low enzyme activity. Individuals with at least one functional CYP3A5*1 allele express the enzyme and thus exhibit increased metabolism of CYP3A5 substrates. These patients often respond poorly to CYP3A5-dependent drugs. Various other alleles lead to reduced activity and may cause adverse drug reaction.
CYP3A4	The enzyme CYP3A is involved in the metabolism of 40% of commonly prescribed drugs. Pathogenic alterations in the CYP3A4 gene can lead to decreased enzyme activity and poor or intermediate metabolizer phenotype. Dose adjustments based on the metabolizer type can reduce side effects.
SLCO1B1	The SLCO1B1 gene encodes the transporter OATP1B1 in the liver. Certain variants in the gene can lead to an altered transport capacity and thus reduce the hepatic absorption of statins. The increased plasma levels increase the risk of statin-induced myopathy, especially when high doses are administered. Dose adjustment based on genotype may reduce side effects.
UGT1A1	The enzyme UDP-glucuronyltransferase is crucially involved in the degradation of the active substance Irinotecan into its metabolite. Variants in the gene lead to reduced enzyme activity. Slow metabolizers for UGT1A1 have an increased risk of developing severe side effects during therapy. The genotyping of UGT1A1*28 and *6 allele is recommended by the BfArM.
TPMT	The enzyme thiopurine S-methyltransferase is involved in the degradation of thiopurines such as azathioprine. Pathogenic variants in the TPMT gene lead to an enzyme deficiency and an accumulation of thioguanine nucleotides in the hematopoietic tissue, which can result in severe myelosuppression. Dose adjustments based on the TPMT genotype can reduce side effects.
NUDT15	The enzyme nudix hydrolase 15 is involved in the degradation of thiopurines such as mercaptopurine and azathioprine. Pathogenic variants in the NUDT15 gene lead to an enzyme deficiency and an accumulation of thioguanine nucleotides in the hematopoietic tissue, which can result in severe myelosuppression with a potentially fatal outcome. Dose adjustments based on the NUDT15 genotype can reduce side effects.
IFNL3	The IFNL3-C/T polymorphism rs12979860 in the human genome is associated with efficacy (SVR = "Sustained Virological Response"). Patients with the C/C genotype respond better to IFN/RBV therapy than patients with the T allele. In addition, carriers of the C/C genotype have a higher rate of spontaneous remission of the disease.
ABCG2	ABCG2 (BCRP) is an ABC transporter that plays an important role in the intestinal absorption and biliary excretion of drugs and their metabolites. Certain variants of the gene can lead to an altered transport capacity and impaired ABCG2 function that may contribute to variable bioavailability and pharmacological response of ABCG2 substrates.

COMT	Catechol-O-methyltransferase is involved in the inactivation of catecholaminergic neurotransmitters such as dopamine and norepinephrine, thereby regulating the amount of these substances available in the body. The COMT-108/158 polymorphism has an influence on the enzyme activity and thus on the efficacy and tolerability of catecholamine-containing drugs.
ABCB1	As an integral component of the cell membrane, the P-glycoprotein mediates the energy-dependent transport of substrates out of the cell to protect against toxic substances. The polymorphism in the ABCB1 gene correlates with gene expression and thus with the amount of PGP and therefore influences the bioavailability of drugs, which has an impact on their efficacy and tolerability.
CYP1A2	The enzyme CYP1A2 is involved in the metabolism of various drugs. Differences in metabolic capacity are mostly due to enzyme inhibition or induction. The CYP1A2*1F allele is associated with increased enzyme inducibility and accelerated metabolism of CYP1A2 substrates. Knowledge of the CYP1A2 genotype can be used for dose adjustment during therapy with CYP1A2-dependent drugs.
ALDH2	The genetic variants p.(Arg48His) in the ADH1B gene and p.(Glu504Lys) in the ALDH2 gene lead to increased enzyme activity of alcohol dehydrogenase 2 and absent enzyme activity and acetaldehyd hydroylase 2, respectively. Therefore, alcohol is increasingly converted into acetaldehyde or the breakdown of acetaldehyde is inhibited. Both mechanisms lead to accumulation of the toxic metabolite acetaldehyd and are associated with alcohol intolerance.
CYP2C19	The enzyme CYP2C19 is involved in the oxidative metabolism of numerous drugs. Different genetic variants lead to either a loss, a reduction or an increase in enzyme activity. Genotyping of the patient can be included in therapy planning to assess efficacy and tolerability. For mavacamten, this is prescribed by the manufacturer.
CYP2C8	Variants in the CYP2C8 gene can lead to reduced enzyme activity and thus slower degradation of the drug. Genotyping patients can help to prevent side effects.
DPYD	Dihydropyrimidine dehydrogenase is significantly involved in the degradation of the chemotherapeutic agent 5-fluorouracil and its prodrugs. Variants in the DPYD gene can lead to reduced enzyme activity and thus slower degradation of DPD substrates.
F5	The factor V mutation type Leiden is the most common congenital thrombophilic risk marker. The analyzed genetic variant leads to resistance to activated protein C and to an elevated risk of thrombosis.
F2	The analyzed factor 2 variant is a thrombophilic risk marker leading to an elevated risk of thrombosis.
CYP4F2	The enzyme CYP4F2 catalyzes the NADPH-dependent oxidation of different metabolic processes, like the oxidation of fatty acids, vitamin K and E, leukotrien and arachidonic acids. Variants in the CYP4F2 gene are associated with dose dependent efficacy and tolerability of warfarin.
VKORC1	This gene encodes the catalytic subunit of the vitamin K epoxide reductase complex, which is responsible for the reduction of inactive vitamin K 2,3-epoxide to active vitamin K in the membrane of the endoplasmic reticulum. Variants in this gene are associated with an increased resistance or sensitivity to warfarin, an inhibitor of vitamin K epoxide reductase.
G6PD	G6PD deficiency (favism) is an X-linked recessive metabolic disorder caused by pathogenic variants in the G6PD gene. Since the reduction equivalents normally produced by the enzyme, such as NADPH, can no longer be fully formed, the erythrocyte membranes are no longer protected from oxidative damage. Depending on the residual activity of the enzyme, this leads to varying degrees of hemolytic anemia.
CYP1A1	The enzyme CYP1A1 plays a key role in the metabolism of environmental toxins and certain drugs. It is known for metabolizing polycyclic aromatic hydrocarbons (PAHs), such as benzo[a]pyrene, as well as hormones like estrogen. Genetic variants of CYP1A1 are associated with increased enzyme inducibility and enhanced substrate metabolism.
BCHE	The enzyme BCHE (butyrylcholinesterase), also known as pseudocholinesterase, is involved in the metabolism of muscle relaxants like succinylcholine and mivacurium, as well as local anesthetics such as procaine. Genetic variants of BCHE can significantly affect enzyme activity. The A- and K-variant are associated with reduced enzyme activity, which may lead to prolonged drug effects and increased sensitivity to certain anesthetics.

Methods

This pharmacogenomic (PGx) test combines short- and long-read sequencing technologies to detect genetic variants relevant to drug metabolism and therapeutic response. CYP2D6 and CYP2D7 are amplified using a long-range PCR, followed by an index PCR step which includes indexes and adapters for PacBio sequencing. The HiFi amplicon primers are designed to capture structural variation affecting CYP2D6, including:

- the full gene and downstream region of CYP2D6
- CYP2D6 upstream duplications
- the full CYP2D7 gene
- CYP2D6-CYP2D7 hybrids
- CYP2D7-CYP2D6 hybrids

To analyze the additional pharmacogenes, target regions are amplified using multiplex PCR and sequenced via Illumina short-read technology. This process includes: Multiplex PCR for target amplification, partial digestion of single stranded nucleotides, end repair and dA tailing, and adapter ligation followed by index PCR.
This combined approach enables high-resolution detection of single nucleotide variants (SNVs), small insertions/deletions (InDels), and known star alleles across clinically relevant pharmacogenes.

Limitations

The report is generated using PharmCAT, which is capable of calling star alleles and providing drug recommendations for the following genes: ABCG2, CYP2B6, CYP2C19, CYP2C9, CYP3A4, CYP3A5, CYP4F2, DPYD, G6PD, IFNL3, NUDT15, SLCO1B1, TPMT, UGT1A1 and VKORC1. ABCB1, ALDH2, BCHE, COMT, CYP1A1, CYP1A2, CYP2C8, CYP2D6, F2 and F5 are called outside of PharmCAT using a customized pipeline. The current protocol does not support detection of the *28 allele in UGT1A1.

Structural variants in genes other than CYP2D6/CYP2D7 are not detectable with this pipeline, including (but not limited to): CYP2B6*29, CYP2B6*30, CYP2C19*36, CYP2C19*37, CYP4F2*16, SLCO1B1*48, SLCO1B1*49

Our sequencing protocol does not provide full gene coverage, except for CYP2D6. This means that not all genetic positions within a gene are analyzed. Consequently, we report all possible genotypes (star alleles) based on the subset of positions available from the sequencing data. For certain genes, multiple star alleles may share the same nucleotide changes at specific positions, and can therefore correspond to several possible star alleles. In such cases, a definitive phenotype prediction cannot be provided. To accurately determine the phenotype in those cases, a follow-up analysis may be ordered. The list of analyzed positions is provided on the chapter 'Analyzed Genes and Variants'.

The list of drugs covered in this report is not comprehensive. Only drugs with established prescribing guidelines are included, but other drugs with similar mechanisms of action may also be affected by the identified variants.

Interpretation and clinical use

PGx preventive screening provides insight into how genetic variants may influence drug metabolism, efficacy, and the risk of adverse effects. It supports the personalization of medication selection and dosing, particularly in areas such as cardiology, psychiatry, pain management, and geriatrics. However, drug response is influenced by multiple factors. Age, organ function, comorbidities, lifestyle, and drug interactions must also be considered. The results obtained with this preventive test should be interpreted by qualified healthcare professionals and used to support clinical judgment. **Patients should not change or stop medications without medical consultation.**

Disclaimers

This PGx test is designed for preventive screening and wellness purposes. It is not a diagnostic test and does not confirm or rule out any disease. Results are not medically validated before release and must be interpreted by a qualified healthcare professional. The report provides genotype-based insights to support informed prescribing decisions. The test is conducted in an ISO 15189-accredited laboratory using validated sequencing methods. It complies with EU IVDR, GDPR, and German GenDG regulations. Test results are provided exclusively with patient consent and are intended for use by healthcare professionals.

References

Table 5: List of References

PMID	Reference title
35152405	The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and Statin-Associated Musculoskeletal Symptoms., Clinical pharmacology and therapeutics, 2022
31006110	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2B6 and Efavirenz-Containing Antiretroviral Therapy., Clinical pharmacology and therapeutics, 2019
25974703	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors., Clinical pharmacology and therapeutics, 2015
37032427	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants., Clinical pharmacology and therapeutics, 2023
None	FDA Table of Pharmacogenetic Associations, None, -1
23486447	Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clinical pharmacology and therapeutics, 2013
27997040	Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update., Clinical pharmacology and therapeutics, 2017
21716271	Clinical Pharmacogenetics Implementation Consortium guidelines for cytochrome P450-2C19 (CYP2C19) genotype and clopidogrel therapy., Clinical pharmacology and therapeutics, 2011
23698643	Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update., Clinical pharmacology and therapeutics, 2013
35034351	Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2C19 Genotype and Clopidogrel Therapy: 2022 Update., Clinical pharmacology and therapeutics, 2022
32770672	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing., Clinical pharmacology and therapeutics, 2021
27981572	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for CYP2C19 and Voriconazole Therapy., Clinical pharmacology and therapeutics, 2017
32189324	Clinical Pharmacogenetics Implementation Consortium Guideline (CPIC) for CYP2C9 and Nonsteroidal Anti-Inflammatory Drugs., Clinical pharmacology and therapeutics, 2020
25099164	Clinical pharmacogenetics implementation consortium guidelines for CYP2C9 and HLA-B genotypes and phenytoin dosing., Clinical pharmacology and therapeutics, 2014
32779747	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and HLA-B Genotypes and Phenytoin Dosing: 2020 Update., Clinical pharmacology and therapeutics, 2021
21900891	Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C9 and VKORC1 genotypes and warfarin dosing., Clinical pharmacology and therapeutics, 2011
28198005	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Pharmacogenetics-Guided Warfarin Dosing: 2017 Update., Clinical pharmacology and therapeutics, 2017
30801677	Clinical Pharmacogenetics Implementation Consortium Guideline for Cytochrome P450 (CYP)2D6 Genotype and Atomoxetine Therapy., Clinical pharmacology and therapeutics, 2019
22205192	Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for codeine therapy in the context of cytochrome P450 2D6 (CYP2D6) genotype., Clinical pharmacology and therapeutics, 2012

24458010	Clinical Pharmacogenetics Implementation Consortium guidelines for cytochrome P450 2D6 genotype and codeine therapy: 2014 update., Clinical pharmacology and therapeutics, 2014
33387367	Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy., Clinical pharmacology and therapeutics, 2021
28002639	Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6 genotype and use of ondansetron and tropisetron., Clinical pharmacology and therapeutics, 2017
29385237	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and Tamoxifen Therapy., Clinical pharmacology and therapeutics, 2018
25801146	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for CYP3A5 Genotype and Tacrolimus Dosing., Clinical pharmacology and therapeutics, 2015
23988873	Clinical Pharmacogenetics Implementation Consortium guidelines for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing., Clinical pharmacology and therapeutics, 2013
29152729	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing: 2017 Update., Clinical pharmacology and therapeutics, 2018
24787449	Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for rasburicase therapy in the context of G6PD deficiency genotype., Clinical pharmacology and therapeutics, 2014
36049896	Expanded Clinical Pharmacogenetics Implementation Consortium Guideline for Medication Use in the Context of G6PD Genotype., Clinical pharmacology and therapeutics, 2023
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