Name:	Surname, Name
Birth:	DD.MM.YYYY
Sex:	Female
Sample ID:	00000

Sampling date:	DD.MM.YYYY
Entry date:	DD.MM.YYYY

MEDICOVER GENETICS

Pharmacogenomics (PGx) Report

Medicover Pharma Passport

Gene	Genotype	Functionality per Allele	Expected phenotype
ABCB1	rs1045642 variant (C)/rs1045642 variant (C)	High expression/High expression	High transport capacity
ABCG2	rs2231142 reference (G)/rs2231142 reference (G)	Normal function/Normal function	Normal Function
ADH1B	*1/*1	Normal function/Normal function	Normal Metabolizer
ALDH2	*1/*1	Normal function/Normal function	Normal Metabolizer
BCHE	Reference/Reference	Normal function/Normal function	Normal Metabolizer
COMT	rs4680 reference (G)/rs4680 variant (A)	High activity/Low activity	Intermediate Activity
CYP1A2	*1/*1	Normal function/Normal function	Normal Metabolizer
CYP2A6	*1/*9,*1/*13,*1/*15,*1/*S4, *1/*S5	Normal function/Ambiguous	Ambiguous
CYP2B6	*1/*18	Normal function/No function	Intermediate Metabolizer
CYP2C19	*1/*2	Normal function/No function	Intermediate Metabolizer
CYP2C8	*1/*4	Normal function/Decreased function	Intermediate Metabolizer
CYP2C9	*1/*9	Normal function/Normal function	Normal Metabolizer (AS:2.0)
CYP2D6	CYP2D6*1/*17	Normal function/Decreased function	Normal Metabolizer (AS:1.5)
CYP3A4	*1/*1	Normal function/Normal function	Normal Metabolizer
CYP3A5	*1/*7	Normal function/No function	Intermediate Metabolizer
CYP4F2	*1/*2	Normal function/Unknown	Unknown
DPYD	c.85T C (*9A) (heterozygous)	Normal function/Normal function	Normal Metabolizer (AS:2.0)
F2	rs1799963 reference (G)/rs1799963 reference (G)	Normal function/Normal function	Normal Function

Gene	Genotype	Functionality per Allele	Expected phenotype
F5	rs6025 reference (C)/rs6025 reference (C)	Normal function/Normal function	Normal Function
G6PD	A- 202A_376G/A- 202A_376G	III/Deficient / III/Deficient	Deficient
NUDT15	*1/*1	Normal function/Normal function	Normal Metabolizer
SLCO1B1	***37/*41**;*27/*41;*24/*41; *41/*52;*41/*56;*41/*57	Normal 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)	Normal coumarin sensitivity/Normal coumarin sensitivity	-1639 GG

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

Legend (result states)

- **Bold diplotype**: this diplotype was selected from multiple possible diplotypes because it had the highest expected population frequency based on the configured allele-frequency resource.
- **Normal/Intermediate/Rapid/Poor/Ultrarapid ...**: predicted phenotype derived from allele functionality.
- **Deficient**: a deficiency phenotype/status was reported for this gene (e.g. G6PD deficiency).
- **Unknown**: no phenotype or functionality annotation is available from the current source. This does not by itself indicate a failed genotype call; failed genotype calls are shown as NOCALL.
- **Ambiguous**: multiple conflicting calls for the same gene (e.g., multiple candidate diplotypes or conflicting functional annotations). Interpretation may require review.
- **Reference**: wild-type sequence.
- **AS:x.y**: activity score appended where available from database.

Dose Recommendations

Dose recommendations derived from PharmCAT v3.4.0 guideline annotations (CPIC, DPWG, FDA). PharmCAT/ClinPGx data version: 2026-07-13-11-40. Allele definitions: source CLINPGX, version 2026-07-13-11-40. Phenotype version: 2026-07-13-11-40. Dose recommendation content is based on external guideline annotations. Medicover is not responsible for the content of these external guideline annotations.

Table 2: Dosing recommendations for drugs related to analyzed genes and genotypes

Drug & Gene	Recommendations	Actionable
Drug: allopurinol **Gene**: ABCG2 **Guideline**: DPWG	The guideline does not provide a recommendation for allopurinol in patients with the the ABCG2 rs2231142 GG genotype (c.421CC; p.141QQ). (**PMID**: *36056234*)	No
Drug: efavirenz **Gene**: CYP2B6 **Guideline**: CPIC	Consider initiating efavirenz with decreased dose of 400 mg/day. (**PMID**: *31006110*)	Yes

Drug & Gene	Recommendations	Actionable
Drug: sertraline **Gene**: CYP2B6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. Consider a slower titration schedule and lower maintenance dose than normal metabolizers. (**PMID**: *25974703*; **PMID**: *37032427*)	Yes
Drug: amitriptyline **Gene**: CYP2C19 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: brivaracetam **Gene**: CYP2C19 **Guideline**: FDA	Results in higher systemic concentrations. Dosage reduction may be necessary. Refer to FDA labeling for specific dosing recommendations. (FDA Table of Pharmacogenetic Associations)	Yes
Drug: citalopram **Gene**: CYP2C19 **Guideline**: CPIC	Initiate therapy with recommended starting dose. Consider a slower titration schedule and lower maintenance dose than normal metabolizers. (**PMID**: *25974703*; **PMID**: *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. (FDA Table of Pharmacogenetic Associations)	Yes
Drug: clomipramine **Gene**: CYP2C19 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: clopidogrel **Gene**: CYP2C19 **Guideline**: CPIC	No automated recommendation is reported because multiple candidate recommendation records for clopidogrel / CYP2C19 / CPIC could not be resolved deterministically.	Not determined
Drug: dexlansoprazole **Gene**: CYP2C19 **Guideline**: CPIC	Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy. (**PMID**: *32770672*)	Yes
Drug: doxepin **Gene**: CYP2C19 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: escitalopram **Gene**: CYP2C19 **Guideline**: CPIC	Initiate therapy with recommended starting dose. Consider a slower titration schedule and lower maintenance dose than normal metabolizers. (**PMID**: *25974703*; **PMID**: *37032427*)	Yes
Drug: imipramine **Gene**: CYP2C19 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: lansoprazole **Gene**: CYP2C19 **Guideline**: CPIC	Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy. (**PMID**: *32770672*)	Yes

Drug & Gene	Recommendations	Actionable
Drug: mavacamten **Gene**: CYP2C19 **Guideline**: DPWG	No action is required for this gene-drug interaction. (No PMID available)	No
Drug: omeprazole **Gene**: CYP2C19 **Guideline**: CPIC	Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy. (**PMID**: *32770672*)	Yes
Drug: pantoprazole **Gene**: CYP2C19 **Guideline**: CPIC	Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy. (**PMID**: *32770672*)	Yes
Drug: sertraline **Gene**: CYP2C19 **Guideline**: CPIC	Initiate therapy with recommended starting dose. Consider a slower titration schedule and lower maintenance dose than normal metabolizers. (**PMID**: *25974703*; **PMID**: *37032427*)	Yes
Drug: trimipramine **Gene**: CYP2C19 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: voriconazole **Gene**: CYP2C19 **Guideline**: CPIC	Initiate therapy with recommended standard of care dosing. (**PMID**: *27981572*)	No
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: 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*; **PMID**: *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 & Gene	Recommendations	Actionable
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*; **PMID**: *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: siponimod **Gene**: CYP2C9 **Guideline**: DPWG	The guideline does not provide a recommendation for siponimod in normal metabolizers. (No PMID available)	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	Please follow the flow chart in figure 2 of the CPIC warfarin guideline to determine the appropriate dosing recommendation. (**PMID**: *21900891*; **PMID**: *28198005*)	Yes
Drug: amitriptyline **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: aripiprazole **Gene**: CYP2D6 **Guideline**: DPWG	The guideline does not provide a recommendation for aripiprazole in normal metabolizers. (**PMID**: *21412232*; **PMID**: *37002327*)	No
Drug: atomoxetine **Gene**: CYP2D6 **Guideline**: CPIC	Initiate with a dose of 40 mg/day and increase to 80 mg/day after 3 days. If no clinical response and in the absence of adverse events after 2 weeks, consider increasing dose to 100 mg/day. If no clinical response observed after 2 weeks, consider obtaining a peak plasma concentration (1 to 2 hours after dose administered). If <200 ng/mL, consider a proportional increase in dose to approach 400 ng/mL. Dosages greater than 100 mg/day may be needed to achieve target concentrations. (**PMID**: *30801677*)	Yes
Drug: brexpiprazole **Gene**: CYP2D6 **Guideline**: DPWG	The guideline does not provide a recommendation for brexpiprazole in normal metabolizers. (**PMID**: *37002327*)	No
Drug: clomipramine **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: codeine **Gene**: CYP2D6 **Guideline**: CPIC	Use codeine label recommended age- or weight-specific dosing. (**PMID**: *22205192*; **PMID**: *24458010*; **PMID**: *33387367*)	No

Drug & Gene	Recommendations	Actionable
Drug: desipramine **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: doxepin **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: eliglustat **Gene**: CYP2D6 **Guideline**: DPWG	The guideline does not provide a recommendation for eliglustat in normal metabolizers. (No PMID available)	No
Drug: flecainide **Gene**: CYP2D6 **Guideline**: DPWG	The guideline does not provide a recommendation for flecainide in normal metabolizers. (**PMID**: *21412232*)	No
Drug: fluvoxamine **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *25974703*; **PMID**: *37032427*)	No
Drug: gefitinib **Gene**: CYP2D6 **Guideline**: DPWG	The guideline does not provide a recommendation for gefitinib in normal metabolizers. (No PMID available)	No
Drug: haloperidol **Gene**: CYP2D6 **Guideline**: DPWG	The guideline does not provide a recommendation for haloperidol in normal metabolizers. (**PMID**: *21412232*; **PMID**: *37002327*)	No
Drug: hydrocodone **Gene**: CYP2D6 **Guideline**: CPIC	Use hydrocodone label recommended age- or weight-specific dosing. (**PMID**: *33387367*)	No
Drug: imipramine **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: meclizine **Gene**: CYP2D6 **Guideline**: FDA	The FDA label indicates that CYP2D6 genetic variation may contribute to inter-individual variability in meclizine exposure. Monitor for adverse reactions and clinical effect. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: metoprolol **Gene**: CYP2D6 **Guideline**: CPIC	Initiate standard dosing. (**PMID**: *38951961*)	No
Drug: nortriptyline **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No

Drug & Gene	Recommendations	Actionable
Drug: ondansetron **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *28002639*; **PMID**: *41979467*)	No
Drug: paroxetine **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *25974703*; **PMID**: *37032427*)	No
Drug: pimozide **Gene**: CYP2D6 **Guideline**: DPWG	The guideline does not provide a recommendation for pimozide in normal metabolizers. (**PMID**: *37002327*)	No
Drug: propafenone **Gene**: CYP2D6 **Guideline**: DPWG	The guideline does not provide a recommendation for propafenone in normal metabolizers. (**PMID**: *21412232*)	No
Drug: risperidone **Gene**: CYP2D6 **Guideline**: DPWG	The guideline does not provide a recommendation for risperidone in normal metabolizers. (**PMID**: *21412232*; **PMID**: *37002327*)	No
Drug: tamoxifen **Gene**: CYP2D6 **Guideline**: CPIC	Avoid moderate and strong CYP2D6 inhibitors. Initiate therapy with recommended standard of care dosing (tamoxifen 20 mg/day). (**PMID**: *29385237*)	Yes
Drug: tetrabenazine **Gene**: CYP2D6 **Guideline**: FDA	Genotyped patients who are identified as extensive (EMs) or intermediate metabolizers (IMs) of CYP2D6, who need doses of XENAZINE [tetrabenazine] above 50 mg per day, should be titrated up slowly at weekly intervals by 12.5 mg daily, to allow the identification of a tolerated dose that reduces chorea. Doses above 50 mg per day should be given in a three times a day regimen. The maximum recommended daily dose is 100 mg and the maximum recommended single dose is 37.5 mg. If adverse reactions such as akathisia, parkinsonism, depression, insomnia, anxiety or sedation occur, titration should be stopped and the dose should be reduced. If the adverse reaction does not resolve, consideration should be given to withdrawing XENAZINE [tetrabenazine] treatment or initiating other specific treatment. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: tramadol **Gene**: CYP2D6 **Guideline**: CPIC	Use tramadol label recommended age- or weight-specific dosing. (**PMID**: *33387367*)	No
Drug: trimipramine **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *23486447*; **PMID**: *27997040*)	No
Drug: tropisetron **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *28002639*; **PMID**: *41979467*)	No

Drug & Gene	Recommendations	Actionable
Drug: venlafaxine **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *37032427*)	No
Drug: vortioxetine **Gene**: CYP2D6 **Guideline**: CPIC	Initiate therapy with recommended starting dose. (**PMID**: *37032427*)	No
Drug: zuclopenthixol **Gene**: CYP2D6 **Guideline**: DPWG	The guideline does not provide a recommendation for zuclopenthixol in normal metabolizers. (**PMID**: *21412232*; **PMID**: *37002327*)	No
Drug: quetiapine **Gene**: CYP3A4 **Guideline**: DPWG	The guideline does not provide a recommendation for quetiapine in normal metabolizers. (**PMID**: *37002327*)	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. (**PMID**: *25801146*)	Yes
Drug: warfarin **Gene**: CYP4F2 **Guideline**: CPIC	No automated recommendation is reported because the genotype-to-phenotype assignment for CYP4F2 is unresolved (Unknown).	Not determined
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*; **PMID**: *29152729*)	No
Drug: flucytosine **Gene**: DPYD **Guideline**: DPWG	The guideline does not provide a recommendation for flucytosine in patients with a DPYD activity score of 2. (No PMID available)	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*; **PMID**: *29152729*)	No
Drug: tegafur **Gene**: DPYD **Guideline**: DPWG	The guideline does not provide a recommendation for tegafur in patients with a DPYD activity score of 2. (**PMID**: *21412232*; **PMID**: *31745289*)	No
Drug: articaine / epinephrine **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may be more susceptible to methemoglobinemia. If local anesthetics are used, close monitoring for symptoms and signs of methemoglobinemia is recommended. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes

Drug & Gene	Recommendations	Actionable
Drug: Ascorbic acid (vitamin C), plain **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may have an increased risk of hemolysis or hemolytic anemia during treatment with Ascorbic acid (vitamin C), plain. Monitoring, dose adjustment, precautions, or alternative therapy should be considered as described in FDA labeling. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: bupivacaine **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may be more susceptible to methemoglobinemia. If local anesthetics are used, close monitoring for symptoms and signs of methemoglobinemia is recommended. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: chloroquine **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may have an increased risk of hemolysis or hemolytic anemia during treatment with chloroquine. Monitoring, dose adjustment, precautions, or alternative therapy should be considered as described in FDA labeling. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: chlorpropamide **Gene**: G6PD **Guideline**: FDA	The FDA label recommends caution with chlorpropamide in patients with G6PD deficiency and consideration of a non-sulfonylurea alternative. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: dabrafenib **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may have an increased risk of hemolysis or hemolytic anemia during treatment with dabrafenib. Monitoring, dose adjustment, precautions, or alternative therapy should be considered as described in FDA labeling. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: dapsone **Gene**: G6PD **Guideline**: CPIC	Avoid use. (**PMID**: *24787449*; **PMID**: *36049896*)	Yes
Drug: flutamide **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may be more susceptible to methemoglobinemia or related adverse effects during treatment with flutamide. Monitoring should be considered as described in FDA labeling. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: glimepiride **Gene**: G6PD **Guideline**: FDA	The FDA label recommends caution with glimepiride in patients with G6PD deficiency and consideration of a non-sulfonylurea alternative. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: glipizide **Gene**: G6PD **Guideline**: FDA	The FDA label recommends caution with glipizide in patients with G6PD deficiency and consideration of a non-sulfonylurea alternative. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: glyburide **Gene**: G6PD **Guideline**: FDA	The FDA label recommends caution with glyburide in patients with G6PD deficiency and consideration of a non-sulfonylurea alternative. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes

Drug & Gene	Recommendations	Actionable
Drug: hydroxychloroquine **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may have an increased risk of hemolysis or hemolytic anemia during treatment with hydroxychloroquine. Monitoring, dose adjustment, precautions, or alternative therapy should be considered as described in FDA labeling. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: lidocaine / prilocaine **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may be more susceptible to methemoglobinemia. If local anesthetics are used, close monitoring for symptoms and signs of methemoglobinemia is recommended. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: lidocaine and tetracaine **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may be more susceptible to methemoglobinemia. If local anesthetics are used, close monitoring for symptoms and signs of methemoglobinemia is recommended. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: mepivacaine **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may be more susceptible to methemoglobinemia. If local anesthetics are used, close monitoring for symptoms and signs of methemoglobinemia is recommended. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: methylene blue **Gene**: G6PD **Guideline**: CPIC	Avoid use. (**PMID**: *24787449*; **PMID**: *36049896*)	Yes
Drug: moviprep **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may have an increased risk of hemolysis or hemolytic anemia during treatment with moviprep. Monitoring, dose adjustment, precautions, or alternative therapy should be considered as described in FDA labeling. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: nalidixic acid **Gene**: G6PD **Guideline**: FDA	Caution should be observed in patients with glucose-6-phosphate dehydrogenase deficiency. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: nitrofurantoin **Gene**: G6PD **Guideline**: CPIC	Use at standard doses with caution and with close monitoring for anemia. (No PMID available)	Yes
Drug: oxymetazoline and tetracaine **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may be more susceptible to methemoglobinemia. If local anesthetics are used, close monitoring for symptoms and signs of methemoglobinemia is recommended. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: pegloticase **Gene**: G6PD **Guideline**: CPIC	Avoid use. (**PMID**: *24787449*; **PMID**: *36049896*)	Yes

Drug & Gene	Recommendations	Actionable
Drug: primaquine **Gene**: G6PD **Guideline**: CPIC	Avoid primaquine, except in the following cases where established expert consensus guidelines for the treatment of malaria should be followed: (1) Treating Plasmodium vivax or Plasmodium ovale malaria for radical cure of liver-stage infections: 0.75 mg/kg once weekly x8 weeks (WHO) or 45 mg once weekly x8 weeks (CDC) - with close monitoring for hemolysis; (2) Treating Plasmodium falciparum malaria by using primaquine single dose as a gametocytocide at 0.25 mg/kg (WHO) - without need for monitoring for hemolysis. (**PMID**: *36049896*)	Yes
Drug: rasburicase **Gene**: G6PD **Guideline**: CPIC	Avoid use. (**PMID**: *24787449*; **PMID**: *36049896*)	Yes
Drug: ropivacaine **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may be more susceptible to methemoglobinemia. If local anesthetics are used, close monitoring for symptoms and signs of methemoglobinemia is recommended. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: sodium nitrite **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may have an increased risk of hemolysis or hemolytic anemia during treatment with sodium nitrite. Monitoring, dose adjustment, precautions, or alternative therapy should be considered as described in FDA labeling. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: sulfasalazine **Gene**: G6PD **Guideline**: FDA	The FDA label indicates that patients with G6PD deficiency may have an increased risk of hemolysis or hemolytic anemia during treatment with sulfasalazine. Monitoring, dose adjustment, precautions, or alternative therapy should be considered as described in FDA labeling. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: tafenoquine **Gene**: G6PD **Guideline**: CPIC	Avoid use. (**PMID**: *24787449*; **PMID**: *36049896*)	Yes
Drug: tolazamide **Gene**: G6PD **Guideline**: FDA	The FDA label recommends caution with tolazamide in patients with G6PD deficiency and consideration of a non-sulfonylurea alternative. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: tolbutamide **Gene**: G6PD **Guideline**: FDA	The FDA label recommends caution with tolbutamide in patients with G6PD deficiency and consideration of a non-sulfonylurea alternative. Refer to FDA labeling for specific dosing recommendations. (See label for more information.)	Yes
Drug: toluidine blue **Gene**: G6PD **Guideline**: CPIC	Avoid use. (**PMID**: *24787449*; **PMID**: *36049896*)	Yes
Drug: azathioprine **Gene**: NUDT15 **Guideline**: CPIC	Initiate therapy with standard starting dose (e.g., 2 mg/kg/day for autoimmune diseases). During therapy, adjust doses of azathioprine based on disease-specific guidelines. It usually takes at least 2 weeks to reach steady state after each dose adjustment. (**PMID**: *21270794*; **PMID**: *23422873*; **PMID**: *30447069*; **PMID**: *41618934*)	No

Drug & Gene	Recommendations	Actionable
Drug: mercaptopurine **Gene**: NUDT15 **Guideline**: CPIC	Initiate therapy with standard starting dose of mecaptopurine (e.g., 75 mg/m2/day for malignancy or 1.5 mg/kg/day for nonmalignancy). During therapy, adjust the doses of myelosuppressive agents, as per standard clinical practice. It usually takes at least 2 weeks of stable dosing to reach steady state after each dose adjustment. (**PMID**: *21270794*; **PMID**: *23422873*; **PMID**: *30447069*; **PMID**: *41618934*)	No
Drug: thioguanine **Gene**: NUDT15 **Guideline**: CPIC	Initiate therapy with standard starting dose of thioguanine (e.g., 40 mg/m2/day for malignancy). During therapy, adjust the doses of myelosuppressive agents, as per standard clinical practice. It usually takes at least 2 weeks of stable dosing to reach steady state after each dose adjustment. (**PMID**: *21270794*; **PMID**: *23422873*; **PMID**: *30447069*; **PMID**: *41618934*)	No
Drug: atorvastatin **Gene**: SLCO1B1 **Guideline**: CPIC	Prescribe ≤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 >40mg needed for desired efficacy, consider combination therapy (i.e., atorvastatin plus non-statin guideline directed medical therapy). (**PMID**: *35152405*; **PMID**: 30423391)	Yes
Drug: elagolix **Gene**: SLCO1B1 **Guideline**: FDA	No automated recommendation is reported because no candidate recommendation record for elagolix / SLCO1B1 / FDA matched the final prioritized genotype-to-phenotype assignment.	Not determined
Drug: fluvastatin **Gene**: SLCO1B1 **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 >40mg per day. (**PMID**: *35152405*)	Yes
Drug: lovastatin **Gene**: SLCO1B1 **Guideline**: CPIC	Prescribe an alternative statin depending on the desired potency (see Figure 1 of the cited guideline publication for recommendations for alternative statins). If lovastatin therapy is warranted, limit dose to ≤20mg/day. (**PMID**: *35152405*)	Yes
Drug: pitavastatin **Gene**: SLCO1B1 **Guideline**: CPIC	Prescribe ≤ 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 >1mg. If dose >2mg needed for desired efficacy, consider an alternative statin (see Figure 1 of the cited guideline publication for recommendations for alternative statins) or combination therapy (i.e. pitavastatin plus non-statin guideline directed medical therapy). (**PMID**: *35152405*; **PMID**: 30423391)	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 >40mg per day. (**PMID**: *35152405*)	Yes
Drug: rosuvastatin **Gene**: SLCO1B1 **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 >20mg. (**PMID**: *35152405*)	Yes
Drug: simvastatin **Gene**: SLCO1B1 **Guideline**: CPIC	Prescribe an alternative statin depending on the desired potency (see Figure 1 of the cited guideline publication for recommendations for alternative statins). If simvastatin therapy is warranted, limit dose to <20mg/day. (**PMID**: *22617227*; **PMID**: *24918167*; **PMID**: *35152405*)	Yes

Drug & Gene	Recommendations	Actionable
Drug: azathioprine **Gene**: TPMT **Guideline**: CPIC	Initiate therapy with standard starting dose (e.g., 2 mg/kg/day for autoimmune diseases). During therapy, adjust doses of azathioprine based on disease-specific guidelines. It usually takes at least 2 weeks to reach steady state after each dose adjustment. (**PMID**: *21270794*; **PMID**: *23422873*; **PMID**: *30447069* ; **PMID**: *41618934*)	No
Drug: mercaptopurine **Gene**: TPMT **Guideline**: CPIC	Initiate therapy with standard starting dose of mecaptopurine (e.g., 75 mg/m2/day for malignancy or 1.5 mg/kg/day for nonmalignancy). During therapy, adjust the doses of myelosuppressive agents, as per standard clinical practice. It usually takes at least 2 weeks of stable dosing to reach steady state after each dose adjustment. (**PMID**: *21270794*; **PMID**: *23422873*; **PMID**: *30447069* ; **PMID**: *41618934*)	No
Drug: thioguanine **Gene**: TPMT **Guideline**: CPIC	Initiate therapy with standard starting dose of thioguanine (e.g., 40 mg/m2/day for malignancy). During therapy, adjust the doses of myelosuppressive agents, as per standard clinical practice. It usually takes at least 2 weeks of stable dosing to reach steady state after each dose adjustment. (**PMID**: *21270794*; **PMID**: *23422873*; **PMID**: *30447069*; **PMID**: *41618934*)	No
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). (**PMID**: *26417955*)	Yes
Drug: irinotecan **Gene**: UGT1A1 **Guideline**: DPWG	The guideline does not provide a recommendation for irinotecan in normal metabolizers. (**PMID**: *21412232*; **PMID**: *36443464*)	No
Drug: sacituzumab govitecan **Gene**: UGT1A1 **Guideline**: DPWG	The guideline does not provide a recommendation for sacituzumab govitecan in normal metabolizers. (No PMID available)	No
Drug: acenocoumarol **Gene**: VKORC1 **Guideline**: DPWG	The guideline does not provide a recommendation for acenocoumarol in patients with the VKORC1 rs9923231 CC genotype (-1639 GG genotype). (**PMID**: *21412232*)	No
Drug: phenprocoumon **Gene**: VKORC1 **Guideline**: DPWG	The guideline does not provide a recommendation for phenprocoumon in patients with the VKORC1 rs9923231 CC genotype (-1639 GG genotype). (**PMID**: *21412232*)	No
Drug: warfarin **Gene**: VKORC1 **Guideline**: CPIC	Please follow the flow chart in figure 2 of the CPIC warfarin guideline to determine the appropriate dosing recommendation. (**PMID**: *21900891*; **PMID**: *28198005*)	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	Detectable haplotypes
ABCB1	rs1045642	*2
ABCG2	rs2231142,rs72552713	rs2231142 reference (G);rs2231142 variant (T)
ADH1B	rs1229984	*2
ALDH2	rs671	111803962:G>A
BCHE	rs1799807,rs1803274	A-Variant;K-Variant
COMT	rs4680	19963748:G>A
CYP1A2	rs762551,rs56107638	*7;*30
CYP2A6	rs1801272,rs4986891,rs28399433,rs28399447, rs28399454	*2;*6;*11;*17;*26
CYP2B6	rs2279343,rs3211371,rs3745274,rs3826711,rs8192709, rs12721655,rs28399499,rs33926104,rs33973337, rs33980385,rs34097093,rs34223104,rs34284776, rs34826503,rs34883432,rs35303484,rs35773040, rs36056539,rs45482602,rs58871670,rs117872433, rs139801276,rs141666881,rs145884402,rs200238771, rs200458614,rs201500445,rs373489637,rs535039125, rs564083989,rs754621576,rs780991919,rs2516199080, chr19:41009313	*1-*11;*13-*14;*17-*20;*22;*24-*26;*33-*34;*36-*37; *39-*41;*43;*45-*48;*50
CYP2C19	rs3758581,rs4244285,rs4986893,rs6413438,rs12248560, rs17882687,rs17884712,rs17885179,rs28399504, rs41291556,rs55640102,rs55752064,rs56337013, rs57700608,rs58973490,rs72552267,rs72558186, rs118203756,rs118203757,rs118203759,rs138142612, rs140278421,rs145328984,rs192154563,rs367543002, rs367543003,rs370803989,rs375781227,rs1288601658, rs1564656981,rs1564660997	*1-*12;*14-*18;*22-*26;*29-*34;*38-*41
CYP2C8	rs1058930,rs11572080,rs11572103	*2-*4
CYP2C9	rs1057910,rs1799853,rs2256871,rs7900194,rs9332130, rs9332131,rs9332239,rs12414460,rs17847037, rs28371685,rs28371686,rs56165452,rs57505750, rs67807361,rs72558187,rs72558189,rs72558190, rs72558192,rs114071557,rs141489852,rs142240658, rs199523631,rs200183364,rs200965026,rs367826293, rs369745682,rs371055887,rs375805362,rs530507053, rs546318684,rs578144976,rs749060448,rs750820937, rs754487195,rs761033063,rs762239445,rs767284820, rs767576260,rs774550549,rs774607211,rs781583846, rs868182778,rs988617574,rs1216169538,rs1237225311, rs1250577724,rs1274535931,rs1289704600, rs1297714792,rs1304490498,rs1364419386, rs1375956433,rs2031308986,rs2492587526, rs2492634549,rs2493006942,chr10:94938719, chr10:94938788,chr10:94942018,chr10:94949161, chr10:94972183,chr10:94981199	*1-*16;*20-*27;*30-*36;*38-*47;*51-*55;*58;*60;*62-*63;*65-*66;*69;*71-*73;*76-*81;*83;*85-*88
CYP2D6	whole gene (exons + introns)	*1-*15;*1xN;*2xN;*3xN;*4xN;*6xN;*9xN;*10xN;*17-*56;*17xN;*29xN;*35xN;*36xN;*41xN;*43xN;*45xN; *58-*65;*68-*75;*81-*185;*146x2

Gene	Analyzed rsIDs	Detectable haplotypes
CYP3A4	rs3208361,rs4646438,rs4986907,rs4986908, rs4986909,rs4986910,rs4986913,rs4987161, rs12721627,rs12721629,rs35599367,rs55785340, rs55901263,rs57409622,rs67666821,rs67784355, rs72552798,rs113667357,rs138105638,rs145582851, rs756833413,rs774109750,rs1318364992,rs1429705359, chr7:99762054,chr7:99762069	*1-*3;*5-*6;*9-*13;*15-*17;*19-*20;*22-*24;*26;*33-*34;*37-*38;*42-*45;*47-*48
CYP3A5	rs776746,rs10264272,rs28383479,rs41303343, rs55817950	*1;*3;*6-*9
CYP4F2	rs2108622,rs3093105,rs114099324	*1-*4;*7
DPYD	rs1801265,rs1801266,rs1801267,rs1801268,rs3918289, rs3918290,rs17376848,rs55674432,rs56038477, rs61622928,rs67376798,rs72547601,rs72547602, rs72549303,rs72549309,rs72549310,rs75017182, rs78060119,rs80081766,rs114096998,rs139459586, rs140114515,rs140602333,rs141044036,rs142512579, rs143815742,rs145529148,rs147545709,rs148799944, rs150385342,rs186169810,rs200064537,rs201035051, rs202144771,rs764666241	Reference;c.1129-5923C>G;c.1129-5923C>G, c.1236G>A (HapB3);c.1156G>T (*12);c.1180C>T; c.1181G>T;c.1218G>A;c.1260T>A;c.1278G>T; c.1294G>A;c.1314T>G;c.1896T>C;c.1898delC (*3);c.1905+1G>A (*2A);c.1905C>G;c.2623A>C; c.2639G>T;c.2656C>T;c.2657G>A (*9B);c.2846A>T; c.2872A>G;c.2915A>G;c.2921A>T;c.2933A>G; c.295_298delTCAT (*7);c.2977C>T;c.2978T>G; c.2983G>T (*10);c.3049G>A;c.3061G>C;c.3067C>A; c.313G>A;c.61C>T;c.62G>A;c.703C>T (*8); c.85T>C (*9A)
F2	rs1799963	rs1799963 Prothrombin 20210A;rs1799963 reference (G)
F5	rs6025	rs6025 Factor V Leiden (T);rs6025 reference (C)
G6PD	rs1050829,rs1050828,rs137852328,rs76723693, rs137852329,rs137852335,rs137852327,rs137852324, rs76645461,rs137852346,rs137852318,rs72554665, rs137852321,rs782322505,rs5030869,rs137852342, rs398123544,rs137852326,rs137852330,rs78365220, rs781865768,rs137852340,rs370918918,rs137852334, rs137852319,rs398123546,rs137852333,rs137852313, rs137852320,rs137852336,rs72554664,rs137852339, rs782308266,rs137852314,rs5030872,rs5030868, rs137852315,rs34193178,rs74575103,rs371489738, rs782090947,rs137852349,rs137852343,rs782757170, rs137852316,rs137852344,rs137852332,rs78478128, rs137852337,rs137852325,rs137852347,rs137852323, rs137852317,rs5030870,rs137852345,rs782487723, rs782754619,rs181277621,rs137852348,rs137852338, rs782098548,rs137852331,rs137852322,rs138687036, rs267606836,rs267606835,rs782608284,additional chrX positions in G6PD region: 154532231-154546131 (91 positions)	For G6PD,171 variant definitions are detectable. The complete list can be provided upon request.
NUDT15	rs116855232,rs139551410,rs147390019,rs149436418, rs186364861,rs746071566,rs761191455,rs766023281, rs768324690,rs769369441,rs777311140,rs1185228044, rs1202487323,rs1368252918,rs1457579126, rs1950545307,chr13:48037749,chr13:48037849	*1;*3-*21
SLCO1B1	rs2306282,rs2306283,rs4149056,rs11045819, rs34671512,rs55737008,rs55901008,rs56101265, rs56199088,rs59502379,rs61760182,rs74064213, rs77271279,rs139257324,rs140790673,rs141467543, rs145144129,rs200331427,rs200995543,rs373327528	*1-*2;*4-*6;*9-*11;*16;*19;*23;*29;*31;*34;*40-*42;*50;*58
TPMT	rs1142345,rs1800460,rs1800462,rs1800584,rs56161402, rs72552736,rs72552737,rs111901354,rs112339338, rs139392616,rs144041067,rs150900439,rs377085266, rs398122996,rs761990479,rs1256618794	*1-*2;*3A;*3B;*3C;*4;*7-*8;*10;*16;*20;*22;*25;*33-*34;*37;*40-*41;*45-*46

Gene	Analyzed rsIDs	Detectable haplotypes
UGT1A1	rs4148323,rs35350960	*1;*6;*27
VKORC1	rs7294,rs9923231,rs9934438,rs17708472	rs9923231 reference (C);rs9923231 variant (T)

Description of genes analyzed in this study

Table 4: Description of all analyzed genes

Gene	Description
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.
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.
ADH1B	The ADH1B gene encodes the beta subunit of class I alcohol dehydrogenase, an enzyme involved in the conversion of ethanol to acetaldehyde. The p.(Arg48His) variant (ADH1B*2; rs1229984) increases enzyme activity and accelerates this conversion, which can contribute to alcohol intolerance by promoting transient acetaldehyde accumulation after alcohol consumption. This variant is associated with lower alcohol consumption and a reduced risk of alcohol dependence.
ALDH2	The ALDH2 gene encodes mitochondrial aldehyde dehydrogenase 2, which converts acetaldehyde to acetate during alcohol metabolism. The p.(Glu504Lys) variant (ALDH2*2; rs671; historically reported as p.(Glu487Lys)) markedly reduces enzyme activity, resulting in acetaldehyde accumulation after alcohol consumption. This variant is associated with alcohol intolerance, including facial flushing and other adverse reactions to alcohol, which often leads to lower alcohol consumption.
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.
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.
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.
CYP2A6	The enzyme CYP2A6 is involved in the metabolism of nicotine and various drugs. Genetic variants can reduce or abolish enzyme activity and thereby alter the metabolism of CYP2A6 substrates. This analysis covers selected CYP2A6 variants; structural variants and other untested variants are not detected.
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.

Gene	Description
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.
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.
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.
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.
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.
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.
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.
F2	The analyzed factor 2 variant is a thrombophilic risk marker leading to an elevated risk of thrombosis.
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.
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.
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.
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.
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.

Gene	Description
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.
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.

Methods

This pharmacogenomic (PGx) assay combines short-read and long-read sequencing technologies to detect genetic variants that influence drug metabolism and treatment response. The genes CYP2D6 and CYP2D7 are amplified using long-range PCR, followed by indexing PCR including PacBio-compatible indices and adapters. The HiFi amplicon primers are designed to detect structural changes affecting CYP2D6, including:

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

For additional pharmacogenes, target regions are amplified using multiplex PCR and sequenced using Illumina short-read technology. This process includes multiplex target amplification, partial digestion of single-stranded nucleotides, end repair and dA tailing, adapter ligation, and indexing PCR.
This combined approach enables high-resolution detection of single nucleotide variants (SNVs), small insertions/deletions (InDels), and known star alleles in clinically relevant pharmacogenes.
In downstream bioinformatic analysis, ambiguous PharmCAT diplotypes are prioritized using Hardy-Weinberg equilibrium (HWE)-based expected frequencies. For a diplotype $*A/*A$ we use $p(A)^2$, and for $*A/*B$ we use $2 \cdot p(A) \cdot p(B)$, based on star-allele frequencies obtained from ClinPGx.
ClinPGx-derived pharmacogene star-allele frequency resources are used under the terms of the Creative Commons Attribution-ShareAlike 4.0 International License (http://creativecommons.org/licenses/by-sa/4.0/).
For HWE-based prioritization of ambiguous diplotypes, a locally maintained snapshot of ClinPGx biobank frequency data was used (documented sources: UKBB (PharmCAT v2.2.1; Spring 2023), AllOfUs (PharmCAT v2.4.0; v7 cohort)).

Limitations

The report is generated with the PharmCAT tool, which supports star-allele identification and drug recommendation reporting for the following genes: ABCG2, CYP2B6, CYP2C19, CYP2C9, CYP3A4, CYP3A5, CYP4F2, DPYD, F2, F5, G6PD, NUDT15, SLCO1B1, TPMT, UGT1A1, and VKORC1. For VKORC1, PharmCAT provides genotype-based recommendations but no standardized allele functionality or predicted phenotype; the valid genotype is therefore interpreted directly. ABCB1, ADH1B, ALDH2, BCHE, COMT, CYP1A2, CYP2A6, CYP2C8 and CYP2D6 are identified outside PharmCAT using a customized workflow. The current protocol does not support detection of the UGT1A1*28 allele.
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, and SLCO1B1*49.
Our sequencing protocol does not provide complete coverage of all genes except CYP2D6. This means that not all genetic positions across a gene are analyzed. Therefore, we report all possible genotypes (star alleles) based on the subset of positions available in the sequencing data. For some genes, multiple star alleles share the same nucleotide

changes at the analyzed positions and may therefore correspond to several possible genotypes. In such cases, a definitive phenotype assignment may not be possible. Additional confirmatory testing may be required for final clarification. The list of analyzed positions is provided in the section “Analyzed Genes and Variants”.
The list of drugs included in this report is not exhaustive. Only drugs with established prescribing guidance are included, but the identified variants may also affect other drugs with similar mechanisms of action.

Interpretation and clinical use

PGx screening helps identify how genetic variants may influence drug metabolism, drug efficacy, and the risk of adverse drug reactions. It supports personalized drug and dose selection, especially in fields such as cardiology, psychiatry, pain management, and geriatrics. However, drug response is influenced by many factors beyond genetics. Age, organ function, comorbidities, lifestyle, and drug-drug interactions must also be taken into account. The results must be reviewed and interpreted by qualified medical professionals in the context of the patient’s clinical situation before any diagnostic or therapeutic decisions are made. It may serve as a basis for further diagnostic evaluation, but it does not constitute a final medical diagnosis. **Patients should not start, stop, or change medication without consulting a physician.**

Disclaimers

This PGx assay is intended for preventive screening and health-promotion purposes. It is not a diagnostic test and cannot confirm or exclude any disease. The results are not medically validated before release and must be interpreted by qualified healthcare professionals. The report contains genotype-based information intended to support informed prescribing decisions. Testing is performed in an ISO 15189-accredited laboratory using validated sequencing methods. The process is aligned with IVDR, GDPR, and the German GenDG. Test results are released only with patient consent and are intended for use by healthcare professionals.

References

Table 5: List of References

PMID	Reference title
36056234	Dutch pharmacogenetics working group guideline for the gene-drug interaction of ABCG2, HLA-B and Allopurinol, and MTHFR, folic acid and methotrexate., European journal of human genetics : EJHG, 2024
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
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

PMID	Reference title
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
21412232	Pharmacogenetics: from bench to byte–an update of guidelines., Clinical pharmacology and therapeutics, 2011
37002327	Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction between CYP2D6, CYP3A4 and CYP1A2 and antipsychotics., European journal of human genetics : EJHG, 2024
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
38951961	Clinical Pharmacogenetics Implementation Consortium Guideline (CPIC) for CYP2D6, ADRB1, ADRB2, ADRA2C, GRK4, and GRK5 Genotypes and Beta-Blocker Therapy., Clinical pharmacology and therapeutics, 2024
28002639	Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6 genotype and use of ondansetron and tropisetron., Clinical pharmacology and therapeutics, 2017
41979467	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 Genotype and Use of 5-HT 3 Receptor Antagonists: 2026 Update., Clinical pharmacology and therapeutics, 2026
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
31745289	Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction of DPYD and fluoropyrimidines., European journal of human genetics : EJHG, 2020

PMID	Reference title
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
21270794	Clinical Pharmacogenetics Implementation Consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing., Clinical pharmacology and therapeutics, 2011
23422873	Clinical pharmacogenetics implementation consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing: 2013 update., Clinical pharmacology and therapeutics, 2013
30447069	Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2018 Update., Clinical pharmacology and therapeutics, 2019
41618934	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2025 Update., Clinical pharmacology and therapeutics, 2026
35152405	The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and Statin-Associated Musculoskeletal Symptoms., Clinical pharmacology and therapeutics, 2022
22617227	The clinical pharmacogenomics implementation consortium: CPIC guideline for SLCO1B1 and simvastatin-induced myopathy., Clinical pharmacology and therapeutics, 2012
24918167	The clinical pharmacogenetics implementation consortium guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update., Clinical pharmacology and therapeutics, 2014
26417955	Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for UGT1A1 and Atazanavir Prescribing., Clinical pharmacology and therapeutics, 2016
36443464	Dutch pharmacogenetics working group (DPWG) guideline for the gene-drug interaction between UGT1A1 and irinotecan., European journal of human genetics : EJHG, 2023