

PHARMACOGENOMICS - COMPREHENSIVE CLINICAL REPORT

Precision prescribing, encoded.

CLINICALLY ACTIONABLE - CPIC & FDA ALIGNED - PROVIDER-FACING

PATIENT
John Doe

DATE OF BIRTH
1968-08-28

REPORT DATE
2026

SPECIMEN
Buccal Swab

AuraGen Pharmacogenomics

Comprehensive Clinical Report - For Healthcare Provider Use

This report integrates pharmacogenomic results from multi-gene panel testing to support clinical decision-making in medication selection and dosing. Results reflect genotype-predicted phenotypes based on validated variant-to-phenotype algorithms aligned with CPIC, DPWG, and FDA guidelines. This report should be interpreted in the context of the patient's complete clinical picture, current medications, comorbidities, and relevant drug-drug interactions.

Patient Name	John Doe	Report ID	AG-PGX-2026-0001
Date of Birth	1968-08-28	Specimen Type	Buccal Swab
Gender	Male	Ethnicity	Caucasian
Report Date	2026	Panel	Comprehensive PGx + Mental Health
Genes Analyzed	CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, CYP4F2, COMT, DPYD, DRD2,	Method	PCR-based enrichment + NGS; Array-based probe evaluation

Secondary Clinical Findings

CARRIER

UGT1A1 *28/*28

Homozygous - consistent with Gilbert syndrome phenotype. Poor UGT1A1 metabolizer. Elevated risk of drug-induced toxicity with irinotecan, nilotinib, and belinostat.

PATHOGENIC

DPYD *1/*2A

Heterozygous pathogenic variant. DPD activity score = 1. Intermediate metabolizer. Increased risk of severe or fatal toxicity with fluoropyrimidines (5-FU, capecitabine). CPIC recommends 50% dose reduction or alternative therapy.

PATHOGENIC

F5 rs6025 GA

Factor V Leiden - heterozygous. Increased risk of venous thrombosis. Relevant to anticoagulant therapy decisions and perioperative planning.

HLA ALERT

HLA-B *1502

Presence of HLA-B*1502 allele. Significantly elevated risk of Stevens-Johnson syndrome / toxic epidermal necrolysis (SJS/TEN) with carbamazepine, lamotrigine, oxcarbazepine, and phenytoin. Most applicable in Asian populations; genetic counseling recommended.

Metabolizer Status - All Genes

Predicted phenotypes for each pharmacogene based on detected diplotypes. Activity levels inform expected drug metabolism and clinical impact.

CYP1A2 *1A/*1C

Enzyme activity: 

Rapid Metabolizer

Increased CYP1A2 activity. Drugs primarily metabolized by CYP1A2 (clozapine, olanzapine, duloxetine, caffeine) may have reduced plasma levels at standard doses. Prodrugs may have increased active metabolite exposure. Monitor for reduced efficacy.


CYP2B6 *1/*1

Enzyme activity: 

Normal Metabolizer

Normal CYP2B6 enzyme activity. Standard dosing of CYP2B6 substrates expected to achieve therapeutic concentrations. Affected drugs: bupropion, efavirenz, cyclophosphamide, methadone, sertraline.

CYP2C9 *1/*3

Enzyme activity:  **Decreased**

Intermediate Metabolizer

Reduced CYP2C9 activity. Active drugs (NSAIDs, warfarin, phenytoin) may accumulate to higher levels - monitor for adverse effects. Prodrugs converted via CYP2C9 may have reduced efficacy. Warfarin dosing should account for this variant.

CYP2C19 *17/*17

Enzyme activity: 

Ultrarapid Metabolizer

Significantly increased CYP2C19 activity. Prodrugs (clopidogrel, omeprazole, pantoprazole) may have increased conversion - increased therapeutic effect possible. Active drugs (diazepam, escitalopram, citalopram) may have reduced plasma levels.

CYP2D6 *2/*5

Enzyme activity:  **Decreased**

Intermediate Metabolizer

Reduced CYP2D6 activity due to *5 (gene deletion) allele. Affects ~25% of clinically used drugs. TCAs, SSRIs, antipsychotics, opioids (codeine, tramadol) and beta-blockers may accumulate. Tramadol active metabolite exposure is reduced.


CYP3A4 *1/*1

Enzyme activity: 

Normal Metabolizer

Normal CYP3A4 activity. The most abundant hepatic CYP enzyme, metabolising approximately 50% of drugs. Standard dosing expected. No adjustment needed for CYP3A4 substrates based on genetics alone.

CYP3A5 *3/*3

Enzyme activity:  **None/Very Low**

Poor/Non-Expressor

Non-expressor phenotype - most prevalent genotype in Caucasian populations. CYP3A5 does not contribute significantly to drug metabolism in this patient. Tacrolimus dosing guidelines exist (CPIC): standard dosing applies as most guidelines are based on *3/*3 individuals.


CYP4F2 *1/*1

Enzyme activity: 

Normal Activity

Normal CYP4F2 vitamin K epoxide metabolism. Together with CYP2C9, VKORC1, and CYP2C cluster rs12777823, contributes to warfarin dose requirements. CYP4F2 *1/*1 does not require warfarin dose adjustment on this basis.

DPYD *1/*2A

Enzyme activity:  **Decreased**

Intermediate Metabolizer


DPD activity score = 1. CPIC Grade A recommendation: reduce fluoropyrimidine dose by 50%, or select alternative. *2A (rs3918290) splice site variant causes significantly reduced DPD enzyme activity. Applicable to 5-FU, capecitabine, tegafur.

TPMT *1/*3C


Enzyme activity:  **Decreased**

Intermediate Metabolizer


Intermediate thiopurine methyltransferase activity. Increased risk of thiopurine-induced myelosuppression (azathioprine, mercaptopurine, thioguanine). CPIC recommendation: reduce thiopurine dose by 30-70% or increase dosing interval.

UGT1A1 *28/*28Enzyme activity:  **None/Very Low****Poor Metabolizer**

Homozygous *28 - Gilbert syndrome. Severely reduced UGT1A1 glucuronidation activity. Critical for irinotecan: CPIC recommendation is to reduce starting dose by at least one dose level. Elevated unconjugated bilirubin expected. Monitor for toxicity with nilotinib and belinostat.

SLCO1B1 *1A/*1AEnzyme activity: **Normal Function**

Normal OATP1B1 hepatic uptake transporter function. No increased risk of statin-induced myopathy based on SLCO1B1 genotype. Standard dosing for simvastatin, atorvastatin, rosuvastatin and other SLCO1B1 substrates.

VKORC1 rs9923231 GAEnzyme activity:  **Increased****Intermediate Activity**

Heterozygous -1639G>A variant. Reduced vitamin K epoxide reductase activity - lower warfarin dose requirement than homozygous wild-type. This variant, combined with CYP2C9 *1/*3 and CYP3A5 *3/*3, should be factored into warfarin initiation algorithm.

Non-Metabolizer Gene Summary

Pharmacodynamic and transporter gene results affecting drug receptor sensitivity, therapeutic response, and adverse effect risk.

Gene	Result	Phenotype	Clinical Significance
COMT	rs4680 GG (Val/Val)	High Activity	Higher COMT enzyme activity - faster dopamine catabolism in prefrontal cortex. Associated with reduced analgesic response to morphine (Val/Val vs Met/Met). May affect dopaminergic drug response (antipsychotics, dopaminergic agents).
DRD2	rs1799978 AA	Normal Expression	Homozygous wild-type. Normal dopamine D2 receptor expression. No known differential response to antipsychotics based on this variant.
F2	rs1799963 GG	Normal Thrombosis Risk	Wild-type prothrombin gene. Normal risk of Factor II-related thrombosis. Note: F5 rs6025 GA (Factor V Leiden) is present - combined thrombosis risk assessment recommended.
F5	rs6025 GA	Increased Thrombosis Risk	Heterozygous Factor V Leiden. ~3-8x increased venous thromboembolism risk. Clinically relevant to anticoagulation decisions, hormone therapy, perioperative prophylaxis, and oral contraceptive prescribing.
GRIK4	rs1954787 CC	Normal Receptor Function	Wild-type glutamate receptor. GRIK4 genotype was associated with antidepressant response in some studies - normal function suggests standard predicted response.
HLA-A	Negative	Normal Risk	HLA-A*31:01 absent. Normal risk of carbamazepine-related hypersensitivity reactions mediated by this allele. Note: HLA-B*1502 is present - see Secondary Findings.
HLA-B	HLA-B*1502	Elevated Hypersensitivity Risk	HLA-B*1502 allele present. Strong association with SJS/TEN from aromatic anticonvulsants (carbamazepine, phenytoin, lamotrigine, oxcarbazepine). Avoidance recommended unless benefits clearly outweigh risk. Most relevant in Han Chinese and other Asian ancestries.
HTR2A	rs7997012 AA / rs6311 A/G	Mixed Genotype	rs7997012 AA (wild-type) but rs6311 A/G (heterozygous) - partial reduction in HTR2A promoter activity. 5-HT2A receptor function may have modest impact on antidepressant and antipsychotic response.
HTR2C	rs3813929 TT	Protective Influence	Homozygous variant associated with reduced risk of antipsychotic-related weight gain (vs CC/CT). Protective against olanzapine, clozapine, and quetiapine-associated metabolic effects. (Note: X-linked gene - in male patients, single allele applies.)
IFNL4	rs12979860 CC	Normal SVR Likelihood	CC genotype - favorable predicted response to peginterferon-alfa-based hepatitis C therapy. Normal sustained virologic response (SVR) probability.
NUDT15	rs116855232 CC	Normal Metabolizer	Wild-type NUDT15 - no increased risk of thiopurine-induced leucopenia via NUDT15 pathway. TPMT *1/*3C is present and remains the primary thiopurine risk factor for this patient.
OPRM1	rs1799971 GG	Asp/Asp Isoform	GG (Asp/Asp) genotype - reduced mu-opioid receptor sensitivity compared to AA (Asn/Asn). Decreased analgesic response to opioids including morphine, tramadol, and fentanyl predicted. Higher doses may be required but escalation should be clinically guided.
SLC6A4	S/S (La/La)	Low Expression	Serotonin transporter short/short allele - associated with increased risk of adverse effects (headache, nausea, agitation, sexual dysfunction, weight gain) with SSRIs. Reduced response to venlafaxine. Escitalopram, sertraline, and vilazodone have relatively better predicted profiles for this genotype.
POLG	Wild-type (all markers)	Normal Risk	No pathogenic POLG variants detected. Normal mitochondrial DNA polymerase gamma function. No increased risk of valproate-induced hepatotoxicity via POLG pathway.
UGT1A4	rs2011425 CC	Wild-type	Wild-type UGT1A4 - normal glucuronidation of lamotrigine, olanzapine and other UGT1A4 substrates. Standard dosing predicted.

Psychiatry & Mental Health

Drug-gene interactions for psychiatric medications. CYP2D6 Intermediate and SLC6A4 S/S genotypes have the greatest clinical impact in this category.

* **MAJOR** * **MODERATE** * **MINIMAL** * **LIMITED** ! **ADVERSE**

<p>Amitriptyline TCA MAJOR</p> <p>Genes: CYP2D6 CYP2C19</p> <p>CYP2D6 IM + CYP2C19 UM: Complex interaction. Reduced CYP2D6 metabolism offset by ultrarapid CYP2C19 activity. Net effect unpredictable - monitor plasma levels. Consider alternative TCA or use therapeutic drug monitoring (TDM).</p>
<p>Citalopram SSRI MAJOR</p> <p>Genes: CYP2C19 SLC6A4</p> <p>CYP2C19 UM: Markedly reduced citalopram plasma levels. SLC6A4 S/S: Increased adverse effect risk. Dual liability - both efficacy and tolerability are compromised. Consider sertraline or escitalopram.</p>
<p>Clomipramine TCA MAJOR</p> <p>Genes: CYP2D6 CYP2C19</p> <p>CYP2D6 IM + CYP2C19 UM: Unpredictable exposure. TDM strongly recommended if prescribed. CPIC: avoid or use with careful monitoring. High risk of cardiac conduction effects at variable plasma levels.</p>
<p>Imipramine TCA MAJOR</p> <p>Genes: CYP2D6 CYP2C19</p> <p>CYP2D6 IM + CYP2C19 UM: Both primary metabolic pathways are affected. TDM essential if this class is selected. Consider desipramine (CYP2D6 only) with TDM, or a non-TCA antidepressant.</p>
<p>Tramadol Opioid/Analgesic MODERATE</p> <p>Genes: CYP2D6 OPRM1</p> <p>CYP2D6 IM: Reduced conversion to active O-desmethytramadol - decreased analgesic efficacy. OPRM1 Asp/Asp: Further reduced opioid receptor sensitivity. Tramadol is unlikely to provide adequate analgesia. Consider non-opioid alternatives or alternative opioid.</p>
<p>Clopidogrel Antiplatelet MAJOR</p> <p>Genes: CYP2C19</p> <p>CYP2C19 UM: Increased conversion to active metabolite - potential for enhanced platelet inhibition and bleeding risk. FDA and CPIC guidelines note that UM phenotype may alter clinical response. Monitor for bleeding.</p>
<p>Escitalopram SSRI MODERATE</p> <p>Genes: CYP2C19 SLC6A4</p> <p>CYP2C19 UM: Reduced escitalopram exposure at standard doses - consider dose increase. SLC6A4 S/S: risk of adverse effects remains. Better SSRI option than citalopram for this patient despite reduced exposure.</p>
<p>Sertraline SSRI LIMITED</p> <p>Genes: CYP2C19 SLC6A4</p> <p>SLC6A4 S/S: Adverse effect risk (GI, CNS) but sertraline has multi-pathway metabolism. Preferred SSRI option for SLC6A4 S/S vs. citalopram/fluvoxamine. Use as directed with monitoring.</p>

○ Fluoxetine

SSRI

MODERATE

Genes:

CYP2D6

SLC6A4

CYP2D6 IM: Fluoxetine plasma levels may be elevated due to reduced metabolism. SLC6A4 S/S: Increased adverse effect risk. Additionally, fluoxetine is a potent CYP2D6 inhibitor - risk of further phenoconversion of CYP2D6. Avoid if possible.

○ Paroxetine

SSRI

MODERATE

Genes:

CYP2D6

SLC6A4

CYP2D6 IM: Paroxetine accumulation risk - paroxetine is both a CYP2D6 substrate AND potent inhibitor, creating self-inhibition loop. SLC6A4 S/S: Adverse effect risk. Avoid; prefer sertraline for this patient.

○ Aripiprazole

Atypical Antipsychotic

MODERATE

Genes:

CYP2D6

CYP2D6 IM: Aripiprazole and active metabolite dehydro-aripiprazole may accumulate at standard doses. Monitor for dose-dependent side effects. CPIC: consider 25% dose reduction or use with TDM.

○ Risperidone

Atypical Antipsychotic

MODERATE

Genes:

CYP2D6

CYP2D6 IM: Risperidone + 9-OH-risperidone (active) combined exposure may be increased. Monitor for extrapyramidal symptoms and QT prolongation. CPIC: reduce dose or switch to an antipsychotic less dependent on CYP2D6.

○ Haloperidol

Typical Antipsychotic

MODERATE

Genes:

CYP2D6

CYP1A2

CYP2D6 IM: Reduced haloperidol clearance - increased plasma levels. CYP1A2 RM may partially compensate. Monitor for EPS and tardive dyskinesia. TDM recommended.

○ Olanzapine

Atypical Antipsychotic

MINIMAL

Genes:

CYP1A2

HTR2C

CYP1A2 RM: Olanzapine clearance may be increased - reduced steady-state levels. HTR2C TT: Protective against olanzapine-related weight gain. If prescribed, consider higher dose range; weight gain risk is genetically reduced.

* Carbamazepine

Mood Stabilizer/AED

ADVERSE

Genes:

HLA-B

HLA-B*1502 PRESENT. AVOID unless benefit clearly outweighs risk. High risk of SJS/TEN. FDA and CPIC guidance: screen for HLA-B*1502 before prescribing in patients of Asian ancestry. If clinically essential, extreme vigilance for cutaneous reactions in first 3 months.

* Phenytoin

AED

ADVERSE

Genes:

HLA-B

HLA-B*1502 PRESENT. Increased SJS/TEN risk. Avoid unless compelling clinical indication. CYP2C9 *1/*3 also reduces phenytoin clearance - accumulation risk compounds the HLA-B*1502 safety concern.

* Lamotrigine

AED/Mood Stabilizer

ADVERSE

Genes:

HLA-B

HLA-B*1502 PRESENT. Increased SJS/TEN risk with lamotrigine. Use with extreme caution; if prescribed, slow titration per CPIC, monitor closely for skin reactions in first 3 months.

○ Venlafaxine

SNRI

MODERATE

Genes:

CYP2D6

SLC6A4

CYP2D6 IM: Venlafaxine-to-ODV metabolism reduced - altered ratio of parent to active metabolite. SLC6A4 S/S: Decreased therapeutic response predicted. Combination suggests limited benefit; consider duloxetine (less CYP2D6-dependent) instead.

○ Nortriptyline

TCA

MAJOR

Genes:

CYP2D6

CYP2D6 IM: Nortriptyline accumulation predicted. CPIC Grade A recommendation: reduce initial dose, use TDM. Target plasma levels 50-150 ng/mL. One of the better-studied CYP2D6 TCAs - TDM-guided dosing is feasible.

○ Diazepam

Benzodiazepine

MODERATE

Genes:

CYP2C19

CYP2C19 UM: Significantly increased diazepam clearance - reduced plasma levels and shorter duration of effect at standard doses. Dose may need to be increased or frequency adjusted. Monitor sedation response.

Analgesic & Anesthesiology

CYP2D6 Intermediate and OPRM1 Asp/Asp genotypes substantially affect opioid metabolism and receptor sensitivity. Non-opioid alternatives should be considered where clinically appropriate.

* **MAJOR** * **MODERATE** * **MINIMAL** * **LIMITED** ! **ADVERSE**

<p>Morphine Opioid MAJOR</p> <p>Genes: OPRM1 CYP2D6</p> <p>OPRM1 Asp/Asp (GG): Reduced mu-opioid receptor sensitivity - higher dose requirements for equivalent analgesia. Standard dosing may be sub-therapeutic. Monitor pain control; titrate carefully. CYP2D6 IM has minimal direct impact on morphine itself.</p>
<p>Codeine Opioid MAJOR</p> <p>Genes: CYP2D6</p> <p>CYP2D6 IM: Reduced conversion of codeine to active morphine. Significantly reduced analgesic efficacy. CPIC Grade A: avoid codeine - insufficient analgesia likely. Use alternative opioids not dependent on CYP2D6.</p>
<p>Tramadol Opioid/Analgesic MODERATE</p> <p>Genes: CYP2D6 OPRM1</p> <p>Dual liability - see Psychiatry section. Insufficient analgesia predicted. CPIC: use with caution or consider alternative. Avoid for acute moderate-severe pain where reliable analgesia is critical.</p>
<p>Hydrocodone Opioid MODERATE</p> <p>Genes: CYP2D6</p> <p>CYP2D6 IM: Reduced conversion to hydromorphone (active). Decreased analgesic efficacy. Monitor pain control; may require higher doses or alternative opioid. Fentanyl or oxymorphone (non-CYP2D6) are reasonable alternatives.</p>
<p>Oxycodone Opioid MODERATE</p> <p>Genes: CYP2D6</p> <p>CYP2D6 IM: Some reduction in oxymorphone conversion. Oxycodone itself has analgesic activity - impact less severe than codeine/tramadol. Monitor response; consider dose adjustment if inadequate relief.</p>
<p>Fentanyl Opioid MINIMAL</p> <p>Genes: CYP3A4</p> <p>CYP3A4 *1/*1 Normal: Standard fentanyl metabolism expected. Fentanyl is a CYP3A4 substrate - no genetic dose adjustment required. OPRM1 Asp/Asp: Monitor for reduced receptor-level sensitivity.</p>
<p>Celecoxib NSAID/COX-2 MAJOR</p> <p>Genes: CYP2C9</p> <p>CYP2C9 *1/*3 IM: Reduced celecoxib clearance - potential drug accumulation and elevated AUC. Monitor for GI and cardiovascular adverse effects. Consider lower initial dose (e.g., 100mg rather than 200mg). CPIC guidance available.</p>
<p>Ibuprofen NSAID MODERATE</p> <p>Genes: CYP2C9</p> <p>CYP2C9 IM: Modest increase in ibuprofen exposure. Clinically relevant at higher doses. Limit to lowest effective dose; avoid prolonged use. Consider acetaminophen (non-CYP2C9) for regular analgesic use.</p>

Cardiovascular

Warfarin dosing is significantly affected by the combination of CYP2C9 *1/*3 (IM), VKORC1 rs9923231 GA (reduced activity), and CYP3A5 *3/*3. Use a validated PGx dosing algorithm.

* **MAJOR** * **MODERATE** * **MINIMAL** * **LIMITED** ! **ADVERSE**

Warfarin

Anticoagulant

MAJOR

Genes:

CYP2C9 **VKORC1** **CYP3A5** **CYP4F2**

Highly complex multi-gene interaction. CYP2C9 *1/*3: Reduced warfarin clearance - lower dose needed. VKORC1 GA: Reduced vitamin K cycle activity - lower dose needed. CYP3A5 *3/*3: standard. CYP4F2 *1/*1: standard. Net effect: significantly lower warfarin dose requirement predicted. Use CPIC or IWPC algorithm for initiation. Target INR 2.0-3.0 with frequent monitoring.

Clopidogrel

Antiplatelet

MAJOR

Genes:

CYP2C19

CYP2C19 UM: Increased prodrug activation - enhanced antiplatelet effect possible. Some UM patients may have adequate or enhanced response, but clinical evidence is less definitive than for PM phenotype. Monitor for bleeding. FDA label recommends awareness of CYP2C19 status.

Metoprolol

Beta-blocker

MAJOR

Genes:

CYP2D6

CYP2D6 IM: Reduced metoprolol clearance - higher plasma levels at standard doses. Increased risk of bradycardia, fatigue, hypotension. Reduce initial dose; titrate to heart rate/BP response. CPIC recommends dose reduction in IM patients.

Carvedilol

Beta-blocker

MAJOR

Genes:

CYP2D6

CYP2D6 IM: Significantly increased carvedilol exposure. Risk of excessive beta-blockade. Start at lowest dose (3.125mg BID); increase slowly. Consider bisoprolol (not CYP2D6-dependent) as alternative.

Flecainide

Antiarrhythmic

MAJOR

Genes:

CYP2D6

CYP2D6 IM: Reduced flecainide clearance - drug accumulation risk. Narrow therapeutic index - use TDM. CPIC recommends 25-50% dose reduction in IM patients. Monitor ECG for PR/QRS prolongation.

Propafenone

Antiarrhythmic

MAJOR

Genes:

CYP2D6

CYP2D6 IM: Significantly elevated propafenone plasma levels. Narrow therapeutic index. Accumulation increases risk of cardiac arrhythmias, including proarrhythmia. Use TDM and ECG monitoring; consider alternative antiarrhythmic.

Simvastatin

Statin

MINIMAL

Genes:

SLCO1B1 **CYP3A4**

SLCO1B1 *1A/*1A: Normal OATP1B1 function - no increased myopathy risk from transporter genetics. CYP3A4 Normal. Standard simvastatin dosing. No PGx dose adjustment required.

Losartan

ARB

MODERATE

Genes:

CYP2C9

CYP2C9 IM: Reduced activation of losartan to active E-3174 metabolite. Reduced antihypertensive efficacy possible. Monitor blood pressure response; consider dose optimization or switch to irbesartan/valsartan (not CYP2C9-dependent).

Hematology / Oncology

DPYD *1/*2A and UGT1A1 *28/*28 are the most critical findings in this category. Both require dose modification before initiating the relevant agents.

* MAJOR * MODERATE * MINIMAL * LIMITED ! ADVERSE

○ Fluorouracil (5-FU)

Fluoropyrimidine

MAJOR

Genes:

DPYD

DPYD *1/*2A - DPD activity score 1. CPIC Grade A: Reduce starting dose by 50%. *2A (IVS14+1G>A splice variant) causes near-complete loss of one DPYD allele. Risk of severe, life-threatening mucositis, neutropenia, neurotoxicity at standard doses. Consider UGT1A1 co-impact for combination regimens.

○ Capecitabine

Fluoropyrimidine

MAJOR

Genes:

DPYD

DPYD *1/*2A: Same recommendation as 5-FU - 50% dose reduction at initiation. Capecitabine is a prodrug of 5-FU. Severe or fatal toxicity risk at standard doses. Document genetic finding prominently in patient record.

○ Irinotecan

Topoisomerase inhibitor

MAJOR

Genes:

UGT1A1

UGT1A1 *28/*28: Poor glucuronidation of SN-38 (active irinotecan metabolite). Markedly increased SN-38 exposure - severe diarrhea and neutropenia risk. CPIC and FDA: Reduce starting dose for patients receiving moderately high to high doses. Monitor closely; consider dose reduction from 180mg/m² to 100-150mg/m².

○ Mercaptopurine

Thiopurine

MAJOR

Genes:

TPMT **NUDT15**

TPMT *1/*3C IM: Intermediate thiopurine metabolism - accumulation of thioguanine nucleotides. CPIC: Reduce starting dose to 30-70% of standard and titrate. NUDT15 wild-type - TPMT is the primary risk driver. Monitor CBC.

○ Azathioprine

Thiopurine

MAJOR

Genes:

TPMT

TPMT *1/*3C IM: Risk of myelotoxicity. CPIC Grade A: Reduce starting dose to 30-70% of standard dose; allow 2-4 weeks to reach steady state before adjusting. Monitor CBC weekly initially.

○ Thioguanine

Thiopurine

MAJOR

Genes:

TPMT

TPMT *1/*3C IM: Increased thioguanine nucleotide accumulation. Same dosing guidance as azathioprine/mercaptopurine. Reduce dose 30-70%; monitor for myelosuppression.

○ Tamoxifen

Endocrine therapy

MAJOR

Genes:

CYP2D6

CYP2D6 IM: Significantly reduced conversion of tamoxifen to active endoxifen. Endoxifen plasma levels may be 40-60% lower than in NM patients. CPIC: consider aromatase inhibitor as alternative in ER+ breast cancer where CYP2D6 IM phenotype is confirmed. If tamoxifen is used, strong CYP2D6 inhibitors (paroxetine, fluoxetine) must be avoided.

○ Nilotinib TKI

MODERATE

Genes: **UGT1A1**

UGT1A1 *28/*28: Reduced nilotinib glucuronidation. Elevated bilirubin and potential drug accumulation. FDA label recommends monitoring; consider dose reduction for hyperbilirubinemia grade 3+ events.

Gastroenterology

CYP2C19 Ultrarapid Metabolizer status significantly affects proton pump inhibitor (PPI) efficacy. Standard PPI doses may be insufficient for this patient.

* MAJOR * MODERATE * MINIMAL * LIMITED ! ADVERSE

Omeprazole

PPI

MAJOR

Genes:

CYP2C19

CYP2C19 UM: Very rapid omeprazole metabolism - markedly reduced AUC. Standard 20mg dose may provide inadequate acid suppression. For *H. pylori* eradication, significantly reduced efficacy. Consider double-dose (40mg BID), rabeprazole (less CYP2C19-dependent), or vonoprazan where available.

Lansoprazole

PPI

MAJOR

Genes:

CYP2C19

CYP2C19 UM: Significantly reduced lansoprazole exposure. Same clinical concern as omeprazole. Dose increase or alternative PPI recommended for reliable acid suppression.

Pantoprazole

PPI

MODERATE

Genes:

CYP2C19

CYP2C19 UM: Reduced pantoprazole levels. Pantoprazole is somewhat less CYP2C19-dependent than omeprazole/lansoprazole but still affected. Consider dose increase to 80mg or alternative agent.

Rabeprazole

PPI

MINIMAL

Genes:

CYP2C19

Rabeprazole is primarily metabolized non-enzymatically - least affected by CYP2C19 UM phenotype among PPIs. Preferred PPI for this patient when reliable acid suppression is required.

Esomeprazole

PPI

MODERATE

Genes:

CYP2C19

CYP2C19 UM: Reduced esomeprazole exposure. Less CYP2C19-dependent than omeprazole, but still impacted in UM. Rabeprazole preferred.

Ondansetron

5-HT₃ antagonist

MODERATE

Genes:

CYP2D6

CYP2D6 IM: Some increase in ondansetron exposure. Limited clinical impact at standard doses (4-8mg). No dose adjustment recommended for antiemetic use, but be aware of potential for modest QT prolongation at accumulation levels.

Infectious Disease

Key interactions involve CYP2C19 for voriconazole and CYP2D6 for certain antiretrovirals.

* **MAJOR** * **MODERATE** * **MINIMAL** * **LIMITED** ! **ADVERSE**

Voriconazole

Antifungal

MAJOR

Genes:

CYP2C19

CYP2C19 UM: Voriconazole is primarily metabolized by CYP2C19. UM phenotype causes markedly reduced voriconazole plasma levels - risk of treatment failure for invasive fungal infections. CPIC Grade A: avoid voriconazole; use alternative antifungal (isavuconazole, posaconazole). If used, double dose may still be insufficient.

Efavirenz

NNRTI

MODERATE

Genes:

CYP2B6

CYP2B6 *1/*1 Normal: Standard efavirenz dosing appropriate. No dose adjustment required. CYP2B6 mediates primary efavirenz metabolism - normal metabolizer status is favorable.

Atazanavir

PI

MODERATE

Genes:

UGT1A1

UGT1A1 *28/*28: Atazanavir inhibits UGT1A1; in a patient already with reduced UGT1A1 activity, significantly elevated bilirubin (unconjugated hyperbilirubinemia) is expected. Monitor bilirubin; consider alternative PI such as darunavir if jaundice becomes problematic.

Raw Genotype Data - All Markers

Complete listing of all tested variant locations with observed genotypes. Results produced by PCR-based enrichment, next-generation sequencing, and array-based probe evaluation.

Gene	Variant / Marker	Genomic Reference	Genotype	Allele / Diplotype
CYP1A2	rs762551	NM_000761.4:c.-9-154C>A	CC	
CYP1A2	rs2069514	NG_008431.2:g.28338G>A	GA	*1A/*1C
CYP2B6	rs2279343	NM_000767.4:c.785A>G	AG	*1/*4
CYP2B6	rs3211371	NM_000767.4:c.1459C>T	CC	
CYP2B6	rs3745274	NM_000767.4:c.516G>T	GG	
CYP2B6	rs8192709	-	CC	
CYP2B6	rs28399499	NM_000767.4:c.983T>C	AA	
CYP2C9	rs1799853	NM_000771.3:c.430C>T	CC	*1/*3
CYP2C9	rs1057910	NM_000771.3:c.1075A>C	AC	
CYP2C9	rs9332131	NM_000771.3:c.817delA	AA	
CYP2C19	rs12248560	NM_000769.2:c.-806C>T	TT	*17/*17
CYP2C19	rs4244285	NM_000769.2:c.681G>A	GG	
CYP2C19	rs4986893	NM_000769.2:c.636G>A	GG	
CYP2C19	rs28399504	NM_000769.2:c.1A>G	AA	
CYP2D6	rs16947	NM_000106.5:c.886C>T	TT	*2/*5
CYP2D6	rs1065852	NM_000106.5:c.100C>T	CC	
CYP2D6	rs3892097	NM_000106.5:c.506-1G>A	GG	
CYP2D6	rs5030655	NM_000106.5:c.454delT	TT	
CYP2D6	rs5030867	NM_000106.5:c.971A>C	AA	
CYP2D6	rs35742686	NM_000106.5:c.775delA	AA	
CYP3A4	rs2740574	NM_017460.5:c.-392G>A	AA	*1/*1
CYP3A5	rs776746	NM_000777.4:c.219-237G>A	CC	*3/*3
CYP4F2	rs2108622	NM_001082.4:c.1297G>A	GG	*1/*1
COMT	rs4680	NM_000754.3:c.472G>A	GG	Val/Val
DPYD	rs3918290	NM_000110.3:c.1905+1G>A	GA	*1/*2A
DPYD	rs55886062	NM_000110.3:c.1679T>G	TT	
DPYD	rs67376798	NM_000110.3:c.2846A>T	TT	
DRD2	rs1799978	NM_000795.3:c.-585A>G	AA	
F2	rs1799963	NM_000506.4:c.*97G>A	GG	
F5	rs6025	NM_000130.4:c.1601G>A	GA	Factor V Leiden het.
HLA-A	-	Exon 2 interrogation	Negative	*31:01 absent
HLA-B	rs2844682 / rs3909184	Exon 2+3 interrogation	T/T + G/C	*1502 present
HTR2A	rs7997012	NM_000621.4:c.614-2211T>C	AA	
HTR2A	rs6311	-	AG	
HTR2C	rs3813929	NM_000868.3:c.-759C>T	TT	Protective/X-linked
HTR2C	rs1414334	-	GG	
IFNL4	rs12979860	NM_001276254.2:c.151-152G>A	CC	
NUDT15	rs116855232	NM_018283.3:c.415C>T	CC	
OPRM1	rs1799971	NM_000914.4:c.118A>G	GG	Asp/Asp
SLC6A4	5-HTTLPR / rs25531	NM_001045.5	S/S (La/La)	Low expression
SLCO1B1	rs4149056	NM_006446.4:c.521T>C	TT	*1A/*1A
SLCO1B1	rs2306283	NM_006446.4:c.388A>G	AA	
TPMT	rs1142345	NM_000367.3:c.719A>G	AG	*1/*3C
TPMT	rs1800462	NM_000367.3:c.238G>C	GG	
TPMT	rs1800460	NM_000367.3:c.460G>A	GG	
UGT1A1	rs4148323	NM_001072.3:c.862-6536G>A	GG	*28/*28
UGT1A1	rs1976391	NM_001072.3:c.862-9697A>G	GG	
UGT1A4	rs2011425	-	CC	
VKORC1	rs9923231	NM_001311311.1:c.-1639G>A	GA	Intermediate activity
POLG	rs113994095	-	GG	

Gene	Variant / Marker	Genomic Reference	Genotype	Allele / Diplotype
POLG	rs113994097	-	GG	
POLG	rs113994098	-	GG	
CYP2C Cluster	rs12777823	NC_000010.10:g.96405502G>A	GG	Wild-type

Key Actionable Findings - Provider Summary

Prioritized summary of findings requiring clinical action. Listed in order of clinical urgency.

IMMEDIATE ACTION	<p>DPYD *1/*2A - Fluoropyrimidines (5-FU, capecitabine)</p> <p>Before prescribing 5-FU, capecitabine or related fluoropyrimidines: MANDATORY 50% dose reduction per CPIC Grade A recommendation. Standard doses carry risk of severe or fatal toxicity. Document in medication record. Consider UGT1A1 co-impact if irinotecan-based regimens are planned.</p>
IMMEDIATE ACTION	<p>UGT1A1 *28/*28 - Irinotecan; Gilbert Syndrome</p> <p>Irinotecan: Reduce starting dose (e.g., 100-150mg/m² rather than 180mg/m²) for moderate-to-high intensity regimens. Gilbert syndrome diagnosis supported - expect baseline elevated unconjugated bilirubin. Monitor with nilotinib, belinostat, and atazanavir.</p>
IMMEDIATE ACTION	<p>HLA-B *1502 - Aromatic Anticonvulsants</p> <p>AVOID carbamazepine, phenytoin, lamotrigine, and oxcarbazepine unless benefit clearly outweighs SJS/TEN risk. If any of these agents are clinically essential, document informed consent, prescribe lowest effective dose with slowest titration, and monitor skin closely for 3+ months. Genetic counseling consultation recommended.</p>
URGENT	<p>TPMT *1/*3C - Thiopurines (azathioprine, mercaptopurine, thioguanine)</p> <p>Reduce thiopurine starting dose by 30-70% of standard dose. Allow 2-4 weeks for steady state before further adjustment. Monitor CBC weekly for the first month. NUDT15 is wild-type - TPMT remains the primary risk driver.</p>
URGENT	<p>CYP2D6 IM + OPRM1 Asp/Asp - Opioid Analgesics</p> <p>Codeine and tramadol are UNLIKELY TO PROVIDE ADEQUATE ANALGESIA - avoid both. Hydrocodone has reduced efficacy; monitor pain response carefully. Morphine may require higher doses due to OPRM1 reduced receptor sensitivity. Fentanyl (CYP3A4) or buprenorphine (partial agonist) are pharmacogenetically preferred alternatives.</p>
URGENT	<p>CYP2C19 UM - Voriconazole</p> <p>Do not use voriconazole as first-line antifungal therapy. UM phenotype causes drug exposure below therapeutic threshold - treatment failure risk. Use isavuconazole, posaconazole, or echinocandin class as alternatives.</p>
IMPORTANT	<p>CYP2C19 UM - All PPIs</p> <p>Standard PPI doses (omeprazole 20mg, lansoprazole 30mg) will provide inadequate acid suppression. For routine GERD: double standard dose, or switch to rabeprazole (least CYP2C19-dependent). For H. pylori eradication: use rabeprazole-based triple or quadruple therapy. Monitor symptom response.</p>
IMPORTANT	<p>CYP2C9 *1/*3 + VKORC1 GA - Warfarin</p> <p>Lower-than-standard warfarin dose required. Use CPIC or IWPC PGx-guided warfarin initiation algorithm. Initial dose estimate: ~30-40% lower than population average. Frequent INR monitoring during initiation. Avoid strong CYP2C9 inhibitors/inducers without reassessment.</p>
IMPORTANT	<p>CYP2D6 IM - Tamoxifen (if indicated)</p> <p>If tamoxifen is prescribed for ER+ breast cancer, strongly consider aromatase inhibitor as alternative (CPIC recommendation). If tamoxifen is used, AVOID concurrent CYP2D6 inhibitors including paroxetine and fluoxetine. Endoxifen plasma levels will be significantly reduced - consider endoxifen monitoring if tamoxifen is continued.</p>
IMPORTANT	<p>F5 rs6025 GA - Factor V Leiden (Heterozygous)</p> <p>Elevated venous thromboembolism risk (~3-8x baseline). Relevant for: anticoagulation decisions, oral contraceptive prescribing, hormone replacement therapy, surgical prophylaxis, and prolonged immobilization. Consider hematology consultation if thrombosis history or high-risk procedures planned.</p>

NOTE

SLC6A4 S/S - SSRIs

Increased adverse effect risk (headache, nausea, agitation, sexual dysfunction, weight gain) with citalopram, fluoxetine, fluvoxamine, and paroxetine. Reduced response to venlafaxine. Preferred options for this patient: sertraline, escitalopram (despite CYP2C19 UM), or vilazodone. Also note CYP2D6 IM compounds adverse effect profile for fluoxetine and paroxetine.

NOTE

CYP2D6 IM - Psychiatric Medications

Multiple TCAs (amitriptyline, nortriptyline, clomipramine, imipramine) and antipsychotics (aripiprazole, risperidone, haloperidol) will have increased plasma levels. TDM is strongly recommended if any of these agents are prescribed. For antidepressant selection: prefer agents with minimal CYP2D6 dependence (mirtazapine, duloxetine, escitalopram).

Test Methodology and Clinical Disclaimer

Test methods, analytical limitations, and important clinical guidance for interpreting this pharmacogenomic report.

Analytical Methodology

Genomic DNA was analyzed by PCR using probe-based methods to interrogate variant locations listed in the Genotype Results table. CYP2D6 copy number status was assessed at promoter, intron 2, intron 6, and exon 9 sites to detect deletions, duplications/multiplications, and hybrid alleles. Array-based evaluation of multiple molecular probes was used for selected loci. Haplotypes are annotated according to legacy nomenclature (PharmVar/CPIC). Inferred diplotypes are reported using published allele frequency and ethnicity data where direct phasing is not possible. Variant detection sensitivity exceeds 99.9%. Results may be affected by non-autologous blood transfusions, transplant therapies, or DNA quality issues.

Genes and Alleles Interrogated

CYP1A2	*1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W
CYP2B6	*4, *5, *6, *7, *9, *16, *18
CYP2C9	*2, *3, *4, *5, *6, *8, *11
CYP2C19	*2, *3, *4, *4B, *10, *17
CYP2D6	*2, *2A, *3, *4, *4M, *4N, *5, *6, *6C, *7, *8, *9, *10, *11, *12, *13, *14, *15, *17, *18, *19, *20, *29, *31, *34, *35, *36, *39, *41, *42, *59, *63, *64, *65, *68, *69, *70, *91, *109, *114
CYP3A4	*1B, *22
CYP3A5	*3, *6, *7
CYP4F2	*3
DPYD	*2A, Asp949Val, *13
SLCO1B1	*1B, *5, *15, *17, *21
TPMT	*2, *3A, *3B, *3C, *4
UGT1A1	*6, *28
HLA-A/B	HLA-A*31:01; HLA-B*15:02, *57:01, *58:01

Clinical Disclaimer

This report is intended solely for use by a qualified healthcare provider. It does not constitute medical advice and does not replace clinical judgment. The treating provider remains ultimately responsible for all prescribing decisions.

Pharmacogenomic results reflect predicted genotype-drug interactions based on current scientific evidence. They do not account for all factors affecting drug response including drug-drug interactions, renal/hepatic function, age, body composition, comorbidities, and adherence. Gene-drug interaction classifications are aligned with CPIC, DPWG, and the FDA Table of Pharmacogenetic Associations guidelines current at time of report generation. As pharmacogenomics science evolves, annotations may be updated - always consult current CPIC guidelines at cpicpgx.org.

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