Table 1. Actionable pharmacogenes and associated drug effects

Gene	Common drug substrates	Drug effects associated with polymorphisms
CYP2B6	Efavirenz (Desta, et al. 2019)	Higher dose adjusted trough concentrations of efavirenz observed in IMs and PMs
CYP2C19	Clopidogrel, (Lee, et al. 2022)	Clopidogrel is a prodrug; thus, IMs and PMs have an increased risk of therapeutic failure due to decreased concentrations of the active metabolite
	SSRIs (eg., citalopram, escitalopram, sertraline) (Hicks, et al. 2015)	UMs: Increased risk for therapeutic failure; PMs: increased risk for drug related AEs
	TCA tertiary amines (eg., amitriptyline, imipramine) (Hicks, et al. 2017)	UMs: Increased risk for therapeutic failure; PMs: increased risk for drug related AEs
	PPIs (eg., omeprazole, lansoprazole, pantoprazole, dexlansoprazole) (Lima, et al. 2020)	UMs: increased risk for therapeutic failure; PMs may have an increased risk for drug-related AEs, particularly with long-term therapy
	Voriconazole (Moriyama, et al. 2017)	UMs: increased risk for subtherapeutic trough; PMs: increased risk for supratherapeutic trough concentrations and drug-related AEs
CYP2C9	NSAIDS (eg., ibuprofen, celecoxib, meloxicam, piroxicam) (Theken, et al. 2020)	IMs and PMs: increase risk of drug-related AEs
	Warfarin (Johnson, et al. 2017)	PMs: increased risk of bleeding and have lower warfarin dose requirements
	Phenytoin, fosphenytoin (Karnes, et al. 2020)	IMs and PMs: increase risk of drug-related AE, including CNS toxicity due to increase blood levels of phenytoin
CYP2C9 cluster SNP rs12777823	Warfarin	Carriers have increased risk of bleeding and may require dose reductions of 10-25%
CYP2D6	SSRIs (eg., paroxetine, fluvoxamine) (Hicks, et al. 2015)	UMs: increased risk for therapeutic failure; PMs: increased risk for drug-related AEs
	TCA tertiary and secondary amines (eg., amitriptyline, nortriptyline, imipramine, desipramine) (Hicks, et al. 2017)	UMs: Increased risk for therapeutic failure; PMs: increased risk for drug related AEs, including cardiotoxicity
	Tamoxifen (Goetz, et al. 2017)	PMs: increased risk for breast cancer recurrence due to decreased levels of more potent metabolite (endoxifen)
	Atomoxetine (Brown, et al. 2019)	UMs: increased risk for therapeutic failure; PMs: increased risk for drug related AEs; TDM is generally recommended
	Opioids (eg., codeine, tramadol, hydrocodone, oxycodone) (Crews, et al. 2021)	**Codeine and tramadol require conversion to active metabolite:** UMs increased risk for drug-related AEs, including respiratory depression; PMs increased risk for therapeutic failure (no analgesic effect).
	Ondansetron and tropisetron (Bell, et al. 2017)	UMs: increased risk for therapeutic failure (lack of antiemetic effect)
CYP3A5	Tacrolimus (Birdwell, et al. 2015)	EMs and IMs: decreased chance of achieving therapeutic concentrations, may require higher (1.5-2 times) tacrolimus dose
CYP4F2	Warfarin (Johnson, et al. 2017)	Carriers of *CYP4F2* rs2108622 T allele may require a 5% to 10% dose increase
DPYD	5-fluorouracil, capecitabine (Amstutz, et al. 2017)	IMs and PMs: increased risk for severe and potentially fatal drug toxicity
G6PD	Rasburicase (Relling, 2014)	Increased risk for hemolytic anemia with G6DP deficiency
*HLA-A*31:01*	Carbamazepine (Phillips, 2017; Chung, 2016)	Carriers: increased risk for SCAR, including SJS, TEN, MPE, DRESS
*HLA-B *57:01*	Abacavir (Martin, 2012; Chung 2016)	Carriers: increased risk for SCAR, including hypersensitivity
*HLA-B *58:01*	Allopurinol (Hershfield, 2013; Chung 2016)	Carriers: increased risk for SCAR, including SJS, TEN, DIHS

*HLA-B*15:02*	Phenytoin, fosphenytoin, carbazepine, oxcarbzepine (Karnes, 2021; Phillips, 2017; Chung 2016)	Carriers: increased risk for SCAR, including SJS, TEN
NUDT15	Azathiopurine, mercaptopurine, thioguanine (Relling, et al. 2019)	IMs and PMs: increased risk for severe, potentially life-threatening myelosuppression due to increased level of TGN metabolites
SLCO1B1	Simvastatin, pitivastatin, atorvastatin, pravastatin, rosuvastatin, fluvastatin (Cooper-DeHoff, et al. 2022)	SLCO1B1 poor function: increased myopathy risk; greatest risk with simvastatin
TPMT	Azathiopurine, mercaptopurine, thioguanine (Relling, et al. 2019)	IMs and PMs: increased risk for severe, potentially life-threatening myelosuppression due to increased level of TGN metabolites
UGT1A1	Atazanavir (Gammal, et al. 2015)	Increased risk for hyperbilirubinemia with UGT1A1 deficiency
VKORC1	Warfarin	Individuals with ≥ 1 (–1639A) variant allele have an increased risk of bleeding and require progressively lower warfarin doses

AEs, adverse events; DIHS, drug-induced hypersensitivity syndrome; DRESS, drug rash with eosinophilia and systemic symptoms; MPE, maculopapular exanthema; NM, normal metabolizers; PM, poor metabolizer; SCAR, severe cutaneous adverse drug reaction; SNP, single nucleotide polymorphism; SJS, Stevens-Johnson syndrome; SSRI, serotonin reuptake inhibitor; TDM, therapeutic drug monitoring; TEN, toxic epidermal necrosis; TCA, tricyclic antidepressants; TGN, thioguanine nucleotides; UM, ultrarapid metabolizer;