PHARMACOGENETIC CONSIDERATIONS FOR PSYCHOTROPIC DRUGS (Part 1 of 2)

Generic	Brand	Pharmacogenomic Biomarker	Section	Genetic Notes
aripiprazole	**Abilify**	CYP2D6	Dosage and admin	**Poor metabolizers (PMs):** initially reduce dose to ½ the usual dose; adjust based on clinical response. *Concomitant strong CYP3A4 inhibitors:* reduce aripiprazole dose to ¼ the usual dose.
	Abilify Maintena		Dosage and admin	**PMs:** 300mg once monthly. *Concomitant CYP3A4 inhibitors:* 200mg once monthly. See full labeling.
atomoxetine	**Strattera**	CYP2D6	Dosage and admin, Warning/Precaution, Interactions, Clinical pharmacology	**Children and adolescents (PMs ≤70kg) or concomitant strong CYP2D6 inhibitors:** initially 0.5mg/kg/day; titrate to usual target dose of 1.2mg/kg/day after 4wks if needed. **Children and adolescents (PMs >70kg) or concomitant strong CYP2D6 inhibitors in adults:** initially 40mg/day; titrate to usual target dose of 80mg/day after 4wks if needed.
brexpiprazole	**Rexulti**	CYP2D6	Dosage and admin	**PMs:** ½ of usual dose. *Concomitant moderate/strong CYP3A4 inhibitors:* ¼ of usual dose.
carbamazepine	**Equetro**	HLA-B*1502	Boxed Warning, Warning/Precaution	**Chinese ancestry:** studies have found strong association between HLA-B*1502 and the risk of developing SJS/TEN. Test for HLA-B*1502 prior to initiation; avoid use if positive for the HLA-B*1502 allele unless benefits clearly outweigh the risks of serious skin reactions.
	Tegretol			
citalopram	**Celexa**	CYP2C19, CYP2D6	Warning/Precaution, Special populations, Clinical pharmacology	**CYP2C19 PMs, concomitant cimetidine or other CYP2C19 inhibitors, hepatic impairment, or >60yrs:** max 20mg/day due to the risk of QT prolongation. **CYP2D6 PMs and EMs:** levels not significantly different.
clobazam	**Onfi**	CYP2C19	Dosage and admin	**PMs:** initially 5mg/day; titrate according to weight but to ½ the usual dose, an additional titration to max dose (20mg/day or 40mg/day, depending on weight) may be started at Day 21.
chlordiazepoxide/amitriptyline	—	CYP2D6	Warning/Precaution	**PMs:** normal metabolizers (NMs) may resemble PMs since certain drugs inhibit CYP2D6. Caution with concomitant SSRIs or when switching from one class to the other. Sufficient time (at least 5wks) must elapse before initiating TCAs in patients being withdrawn from fluoxetine. *Concomitant CYP2D6 inhibitors:* may need to adjust dose of either drug; if withdrawn, may need to increase TCA dose (monitor).
clomipramine	**Anafranil**	CYP2D6	Interactions	See chlordiazepoxide/amitriptyline.
clozapine	**Clozaril, FazaClo**	CYP2D6	Dosage and admin, Special populations, Clinical pharmacology	**PMs:** may need to reduce dose. Increased clozapine levels possible since it's completely metabolized and then excreted.
desipramine	**Norpramin**	CYP2D6	Interactions	See chlordiazepoxide/amitriptyline.
dextromethorphan/quinidine	**Nuedexta**	CYP2D6	Warning/Precaution, Clinical pharmacology, Interactions	**PMs:** quinidine component does not contribute to the effectiveness of Nuedexta in PMs but a possible risk of significant toxicity is present. Consider genotyping to determine PM status prior to initiation.
doxepin	**Silenor**	CYP2D6, CYP2C19	Special populations	**PMs:** may have higher doxepin plasma levels than NMs.

(continued)

PHARMACOGENETIC CONSIDERATIONS FOR PSYCHOTROPIC DRUGS (Part 2 of 2)

Generic	Brand	Pharmacogenomic Biomarker	Section	Genetic Notes
fluoxetine	**Prozac**	CYP2D6	Interactions, Clinical pharmacology	**Concomitant drugs metabolized by CYP2D6 or narrow therapeutic index:** NMs may resemble PMs since fluoxetine is a CYP2D6 inhibitor. Initiate lowest effective dose if receiving fluoxetine or have taken it in previous 5wks. If already taking drugs metabolized by CYP2D6 and fluoxetine is added afterwards, consider decreasing dose of original drug.
fluoxetine/ olanzapine	**Symbyax**	CYP2D6	Clinical pharmacology	See fluoxetine.
fluvoxamine	**—**	CYP2D6	Interactions	**PMs:** caution with fluvoxamine and other concomitant drugs known to inhibit CYP2D6.
galantamine	**Razadyne**	CYP2D6	Special populations, Clinical pharmacology	**PMs:** similar pharmacokinetics parameters compared to EMs. No dosage adjustment needed in PMs since the dose is individually titrated to tolerability.
iloperidone	**Fanapt**	CYP2D6	Dosage and admin, Clinical pharmacology	**PMs:** higher exposure to iloperidone vs. EMs. Reduce dose by ½. Lab tests are available to identify CYP2D6 PMs.
imipramine	**Tofranil**	CYP2D6	Interactions	See chlordiazepoxide/amitriptyline.
modafinil	**Provigil**	CYP2D6	Interactions, Clinical pharmacology	**PMs:** metabolism by CYP2C19 may be substantially increased. Provigil may cause elevation in tricyclic levels; may need to reduce dose of tricyclics.
nortriptyline	**Pamelor**	CYP2D6	Interactions	See chlordiazepoxide/amitriptyline.
perphenazine	**—**	CYP2D6	Clinical pharmacology, Interactions	**PMs:** metabolize perphenazine slower and have higher concentrations vs. NMs or extensive metabolizers (EMs). **Elderly:** PMs have higher plasma concentrations of antipsychotics at usual doses, which may correlate with the emergence of side effects. Prospective phenotyping prior to initiation may identify those at risk for adverse events.
pimozide	**Orap**	CYP2D6	Dosing and admin, Warning/Precaution	**Children (>0.05mg/kg/day):** perform CYP2D6 genotyping. *PMs:* max 0.05mg/kg/day; should not increase dose earlier than 14 days. **Adults (doses >4mg/day):** perform CYP2D6 genotyping. *PMs:* max 4mg/day; should not increase dose earlier than 14 days.
protriptyline	**Vivactil**	CYP2D6	Warning/Precaution	See chlordiazepoxide/amitriptyline.
risperidone	**Risperdal**	CYP2D6	Clinical pharmacology	EMs and PMs have similar pharmacokinetics even though EMs convert risperidone to 9-hydroxy-risperidone quicker than PMs. **Risperidone EMs half-life:** 3hrs. **Risperidone PMs half-life:** 20hrs. **Overall mean half-life:** 20hrs.
tetrabenazine	**Xenazine**	CYP2D6	Dosage and admin	**>50mg/day:** perform CYP2D6 genotyping to determine PM or EM status prior to initiation. Individualize dose based on PM or EM status. **EMs or intermediate metabolizers (IMs):** max 37.5mg/dose and 100mg/day. **PMs:** max 25mg/dose and 50mg/day.
thioridazine	**—**	CYP2D6	Contraindications	Contraindicated in patients known to have a genetic defect leading to reduced CYP2D6 activity.
trimipramine	**Surmontil**	CYP2D6	Interactions	See chlordiazepoxide/amitriptyline.
valbenazine	**Ingrezza**	CYP2D6	Dosage and admin, Special populations	**PMs:** consider reducing dose based on tolerability. Increased exposure to valbenazine's active metabolite may increase risk of adverse reactions.

NOTES

Not an inclusive list of medications or pharmacogenomic details. Please see drug monograph at www.eMPR.com and/or contact company for full drug labeling.

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