A = Active Alert, N = No Alert

Medication	Alert Type	Gene	Phenotype	Alert Language
5-Fluorouracil	N	**DPYD**	Ultrarapid Metabolizer	
	N		Normal Metabolizer	
	A		Reduced Metabolizer	Consider reducing starting dose by at least 50%, followed by titration based on toxicity or pharmacokinetic test (if available). Level of Evidence: **Moderate.** Reduced metabolizer status predicts increased risk for severe or even fatal drug toxicity when treated with fluoropyrimidine drugs.
	A		Poor Metabolizer	Select alternate drug. Level of Evidence: **Strong.** Poor metabolizer status predicts increased risk for severe or even fatal drug toxicity when treated with fluoropyrimidine drugs

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Medication	Alert Type	Gene	Phenotype CYP2D6	Phenotype CYP2C19	Alert Language
amitriptyline	A	**CYP2D6/CYP2C19**	Ultrarapid Metabolizer	Ultrarapid Metabolizer	Avoid amitriptyline use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6 and CYP2C19. If a amitriptyline is warranted, consider increasing the starting dose and use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**. This patient's ultra-rapid metabolizer status predicts poor amitriptyline efficacy.
	A	**CYP2D6/CYP2C19**	Normal Metabolizer	Ultrarapid Metabolizer	Consider alternative drug not metabolized by CYP2C19. If a amitriptyline is warranted, consider increasing the starting dose and use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Moderate**. This patient's ultra-rapid metabolizer status predicts poor amitriptyline efficacy.
	A	**CYP2D6/CYP2C19**	Reduced Metabolizer	Ultrarapid Metabolizer	Consider alternative drug not metabolized by CYP2C19. If a amitriptyline is warranted, consider increasing the starting dose and use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Moderate**. This patient's ultra-rapid metabolizer status predicts poor amitriptyline efficacy.
	A	**CYP2D6/CYP2C19**	Poor Metabolizer	Ultrarapid Metabolizer	Avoid amitriptyline use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6 and CYP2C19. If a amitriptyline is warranted, consider increasing the starting dose and use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**. This patient's ultra-rapid metabolizer status predicts poor amitriptyline efficacy.
	A	**CYP2D6/CYP2C19**	Ultrarapid Metabolizer	Normal Metabolizer	Avoid amitriptyline use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. If a amitriptyline is warranted, consider increasing the starting dose and use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**. This patient's ultra-rapid metabolizer status predicts poor amitriptyline efficacy.
	N	CYP2D6/CYP2C19	Normal Metabolizer	Normal Metabolizer	
	A	**CYP2D6/CYP2C19**	Reduced Metabolizer	Normal Metabolizer	Consider 25% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong.**
	A	**CYP2D6/CYP2C19**	Poor Metabolizer	Normal Metabolizer	Avoid tricyclic use. Consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**.
	A	**CYP2D6/CYP2C19**	Ultrarapid Metabolizer	Reduced Metabolizer	Avoid amitriptyline use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. If a amitriptyline is warranted, consider increasing the starting dose and use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**.
	N	CYP2D6/CYP2C19	Normal Metabolizer	Reduced Metabolizer	
	A	**CYP2D6/CYP2C19**	Reduced Metabolizer	Reduced Metabolizer	Consider 25% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Moderate**.
	A	**CYP2D6/CYP2C19**	Poor Metabolizer	Reduced Metabolizer	Avoid tricyclic use. Consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**.
	A	**CYP2D6/CYP2C19**	Ultrarapid Metabolizer	Poor Metabolizer	Avoid amitriptyline use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6 and CYP2C19. If a amitriptyline is warranted, consider using therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**.
	A	**CYP2D6/CYP2C19**	Normal Metabolizer	Poor Metabolizer	Consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**.
	A	**CYP2D6/CYP2C19**	Reduced Metabolizer	Poor Metabolizer	Avoid amitriptyline use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6 and CYP2C19. If a amitriptyline is warranted, consider using therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Moderate**.
	A	**CYP2D6/CYP2C19**	Poor Metabolizer	Poor Metabolizer	Avoid amitriptyline use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6 and CYP2C19. If a amitriptyline is warranted, consider using therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**.

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Medication	Alert Type	Gene	Phenotype	Alert Language
aripiprazole	N	**CYP2D6**	Ultrarapid Metabolizer	
	N		Normal Metabolizer	
	N		Reduced Metabolizer	
	A		Poor Metabolizer	Consider 50% reduction of recommended starting aripiprazole dose and adjust dose to clinical response. Level of evidence: **Strong**. This patients poor metabolizer status predicts reduced aripiprazole dose requirements.

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Medication	Alert Type	Gene	Phenotype	Alert Language
atomoxetine	A	**CYP2D6**	Ultrarapid Metabolizer	Be alert to reduced efficacy or select alternative drug (e.g., methylphenidate, clonidine). Level of evidence: **Moderate**.
	N		Normal Metabolizer	
	N		Reduced Metabolizer	
	A		Poor Metabolizer	Consider starting with standard dose (e.g. 40 mg daily) and only increase to the usual target dose (e.g. 80 mg daily) if symptoms fail to improve after 4 weeks and the initial dose is well tolerated.. Level of evidence: **Strong**. This patient's poor metabolizer status predicts higher than expected exposure to atomoxetine and increased risk of adverse events.

A = Active Alert, N = No Alert

Medication	Alert Type	Gene	Phenotype	Alert Language
capecitabine	N	**DPYD**	Ultrarapid Metabolizer	
	N		Normal Metabolizer	
	A		Reduced Metabolizer	Consider reducing starting dose by at least 50%, followed by titration based on toxicity or pharmacokinetic test (if available). Level of Evidence: **Moderate.** Reduced metabolizer status predicts increased risk for severe or even fatal drug toxicity when treated with fluoropyrimidine drugs.
	A		Poor Metabolizer	Select alternate drug. Level of Evidence: **Strong.** Poor metabolizer status predicts increased risk for severe or even fatal drug toxicity when treated with fluoropyrimidine drugs

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Medication	Alert Type	Gene	Phenotype	Alert Language
doxepin		**CYP2D6**	Ultrarapid Metabolizer	If doxepin is prescribed at 25mg or greater, consider an alternate medication. Level of evidence: **Strong**. This patient's poor metabolizer status predicts in increased risk of adverse effects.
			Normal Metabilizer	
			Reduced Metabolizer	If doxepin is prescribed at 25mg or greater, consider a 25% dose reduction. Level of evidence: **Strong**. This patient's reduced metabolizer status predicts reduced doxepin dose requiements.
			Poor Metabolizer	If doxepin is prescribed at 25mg or greater, consider a 60% dose reduction or an alternate medication. Level of evidence: **Strong**. This patient's poor metabolizer status predicts in increased risk of adverse effects.

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Medication	Alert Type	Gene	Phenotype	Alert Language
efavirenz	N	**CYP2B6**	Ultrarapid Metabolizer	
	N		Normal Metabolizer	
	N		Reduced Metabolizer	
	A		Poor Metabolizer	Consider a reduced starting dose (e.g. 400 mg/day) with increased monitoring of viral load and CD4 levels. If the normal 600mg/day dose is prescribed, monitor for efavirenz-associated adverse events, including CNS toxicity. Level of Evidence: **Strong**. This poor metabolizer status predicts higher than expected exposure to efavirenz.

A = Active Alert, N = No Alert

Medication	Alert Type	Gene	Phenotype	Alert Language
esomeprazole	A	**CYP2C19**	Ultrarapid Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's ultra-rapid metabolizer status predicts increased dosing requirement.
	A		Rapid Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's rapid metabolizer status predicts increased dosing requirement.
	A		Normal Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's normal metabolizer status predicts increased dosing requirement.
	A		Reduced Metabolizer	Consider once daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Moderate**. This patient's reduced metabolizer status predicts that this patient may respond to once-daily dosing.
	A		Poor Metabolizer	Consider once daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Moderate**. This patient's poor metabolizer status predicts that this patient may respond to once-daily dosing.

A = Active Alert, N = No Alert

Medication	Alert Type	Gene	Phenotype	Alert Language
lansoprazole	A	**CYP2C19**	Ultrarapid Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's ultra-rapid metabolizer status predicts increased dosing requirement.
	A		Rapid Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's rapid metabolizer status predicts increased dosing requirement.
	A		Normal Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's normal metabolizer status predicts increased dosing requirement.
	A		Reduced Metabolizer	Consider once daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Moderate**. This patient's reduced metabolizer status predicts that this patient may respond to once-daily dosing.
	A		Poor Metabolizer	Consider once daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Moderate**. This patient's poor metabolizer status predicts that this patient may respond to once-daily dosing.

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Medication	Alert Type	Gene	Phenotype	Alert Language
nortriptyline	A	**CYP2D6**	Ultrarapid Metabolizer	Avoid nortriptyline use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. If a nortriptyline is warranted, consider increasing the starting dose and use therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**. This patient's ultra-rapid metabolizer status predicts poor nortriptyline efficacy.
	N		Normal Metabolizer	
	A		Reduced Metabolizer	Consider 25% reduction of recommended starting nortriptyline dose and utilize therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Moderate**. This patient's reduced metabolizer status predicts reduced nortriptyline dose requirements.
	A		Poor Metabolizer	Avoid nortriptyline use or consider 50% reduction of recommended starting nortriptyline dose and utilize therapeutic drug monitoring to guide dose adjustments. Level of evidence: **Strong**. This patient's poor metabolizer status predicts increased risk of adverse effects.

A = Active Alert, N = No Alert

Medication	Alert Type	Gene	Phenotype	Alert Language
omeprazole	A	**CYP2C19**	Ultrarapid Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's ultra-rapid metabolizer status predicts increased dosing requirement.
	A		Rapid Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's rapid metabolizer status predicts increased dosing requirement.
	A		Normal Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's normal metabolizer status predicts increased dosing requirement.
	A		Reduced Metabolizer	Consider once daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Moderate**. This patient's reduced metabolizer status predicts that this patient may respond to once-daily dosing.
	A		Poor Metabolizer	Consider once daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Moderate**. This patient's poor metabolizer status predicts that this patient may respond to once-daily dosing.

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Medication	Alert Type	Gene	Phenotype	Alert Language
pantoprazole	A	**CYP2C19**	Ultrarapid Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's ultra-rapid metabolizer status predicts increased dosing requirement.
	A		Rapid Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's rapid metabolizer status predicts increased dosing requirement.
	A		Normal Metabolizer	Consider twice daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Strong**. This patient's normal metabolizer status predicts increased dosing requirement.
	A		Reduced Metabolizer	Consider once daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Moderate**. This patient's reduced metabolizer status predicts that this patient may respond to once-daily dosing.
	A		Poor Metabolizer	Consider once daily dosing of a proton pump inhibitor for patients with Barret's esophagus or H. pylori. Level of evidence: **Moderate**. This patient's poor metabolizer status predicts that this patient may respond to once-daily dosing.

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Medication	Alert Type	Gene	Phenotype HLA-B*15:02	Phenotype CYP2C9	Alert Language
phenytoin	A	**HLA-B*15:02 and CYP2C9**	**positive**	Ultrarapid Metabolizer	If patient is phenytoin naïve, do not use phenytoin/fosphenytoin. Increased risk of phenytoin-induced SJS/TEN. Level of evidence: **Strong**.
	N		**negative**	Ultrarapid Metabolizer	
	A		**positive**	Normal Metabolizer	If patient is phenytoin naïve, do not use phenytoin/fosphenytoin. Increased risk of phenytoin-induced SJS/TEN. Level of evidence: **Strong**.
	N		**negative**	Normal Metabolizer	
	A		**positive**	Reduced Metabolizer	If patient is phenytoin naïve, do not use phenytoin/fosphenytoin. Increased risk of phenytoin-induced SJS/TEN. Level of evidence: **Strong**.
	A		**negative**	Reduced Metabolizer	Consider 25% reduction of recommended starting maintenance dose Subsequent doses should be adjusted according to therapeutic drug monitoring and response. Level of evidence: **Moderate.** Reduced phenytoin metabolism, higher plasma concentrations will increase probability of toxicities.
	A		**positive**	Poor Metabolizer	If patient is phenytoin naïve, do not use phenytoin/fosphenytoin. Increased risk of phenytoin-induced SJS/TEN. Level of evidence: **Strong**.
	A		**negative**	Poor Metabolizer	Consider 50% reduction of recommended starting maintenance dose Subsequent doses should be adjusted according to therapeutic drug monitoring and response. Level of evidence: **Strong** Reduced phenytoin metabolism, higher plasma concentrations will increase probability of toxicities.

A = Active Alert, N = No Alert

Medication	Alert Type	Gene	Phenotype	Alert Language
rasburicase	N	**G6PD**	Ultrarapid Metabolizer	
Note: X-linked	N		Normal Metabolizer	
	A		Reduced Metabolizer	Consider an alternative agent (e.g. allopurinol). Rasburicase is contraindicated in patients with reduced G6PD activity. G6PD enzyme testing should be performed to confirm patient's G6PD status. Level of Evidence: **Strong**. This patients reduced metabolizer status predicts increased risk of acute hemolytic anemia and possible methemoglobinemia.
	A		Poor Metabolizer	Consider an alternative agent (e.g. allopurinol). Rasburicase is contraindicated in patients with poor G6PD activity. G6PD enzyme testing should be performed to confirm patient's G6PD status. Level of Evidence: **Strong**. This patients poor metabolizer status predicts increased risk of acute hemolytic anemia and possible methemoglobinemia.

A = Active Alert, N = No Alert

Medication	Alert Type	Gene	Phenotype	Alert Language
simvastatin	N	**SLCO1B1**	Ultrarapid Metabolizer	
	N		Normal Metabolizer	
	A		Reduced Metabolizer	Consider a reduced simvastatin starting dose (e.g. 10 to 20 mg/day) or consider an alternative statin (e.g. pravastatin or rosuvastatin). Routine CK surveillance may be warranted. Level of evidence: **Strong**. This patients reduced metabolizer status predicts increased risk of myopathy associated with simvastatin.
	A		Poor Metabolizer	Consider a reduced simvastatin starting dose (e.g. 10 to 20 mg/day) or consider an alternative statin (e.g. pravastatin or rosuvastatin). Routine CK surveillance may be warranted. Level of evidence: **Strong**. This patients poor metabolizer status predicts high risk of myopathy associated with simvastatin.

A = Active Alert, N = No Alert

Medication	Alert Type	Gene	Phenotype	Alert Language
tacrolimus	A	**CYP3A5**	Ultrarapid Metabolizer	Consider increasing the starting dose 1.5 to 2 times the recommended starting dose. Total starting dose should not exceed 0.3mg/kg/day. Use therapeutic drug monitoring to guide dose adjustments. **Strong.** This ultrarapid metabolizer phenotype predicts lower than expected concentrations of tacrolimus.
	A		Normal Metabolizer	Consider increasing the starting dose 1.5 to 2 times the recommended starting dose. Total starting dose should not exceed 0.3mg/kg/day. Use therapeutic drug monitoring to guide dose adjustments. **Strong.** This normal metabolizer status predicts lower than expected concentrations of tacrolimus.
	N		Reduced Metabolizer	
	N		Poor Metabolizer	

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Medication	Alert Type	Gene	Phenotype	Alert Language
venlafaxine	A	**CYP2D6**	Ultrarapid Metabolizer	Consider a normal starting dose and titrating to a maximum of 150% of the standard dose. Level of Evidence: **Strong.** This ultrarapid metabolizer status predicts lower than expected venlafaxine plasma levels at standard doses.
	N		Normal Metabolizer	
	A		Reduced Metabolizer	Select an alternative drug (e.g. citalopram or sertraline) or titrate dose slowly to clinical response and monitor (O-desmethyl)-venlafaxine plasma concentration. Level of evidence: **Strong.** This reduced metabolizer status predicts higher than expected concentrations of venlafaxine.
	A		Poor Metabolizer	Select an alternative drug (e.g. citalopram or sertraline) or titrate dose slowly to clinical response and monitor (O-desmethyl)-venlafaxine plasma concentration. Level of evidence: **Strong**. This poor metabolizer status predicts higher than expected concentrations of venlafaxine.

A = Active Alert, N = No Alert

Medication	Alert Type	Gene	Phenotype	Alert Language
voriconazole	A	**CYP2C19**	Ultrarapid Metabolizer	Consider increasing the dose and increased monitoring. Level of evidence: **Moderate**. This patient's ultrarapid metabolizer statis predicts lack of drug efficacy.
	A		Rapid Metabolizer	Consider increasing the dose and increased monitoring. Level of evidence: **Moderate**. This patient's rapid metabolizer status predicts lack of drug efficacy.
	N		Normal Metabolizer	
	A		Reduced Metabolizer	Consider increased monitoring. Level of evidence: **Moderate**. This patient's reduced metabolizer status predicts that this patient is at increased risk for side effects.
	A		Poor Metabolizer	Consider increased monitoring. Level of evidence: **Moderate**. This patient's poor metabolizer status predicts that this patient is at increased risk for side effects.

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Medication	Alert Type	Gene	Phenotype	Alert Language
warfarin	N	**CYP2C9/VKORC1**	Ultrarapid Metabolizer	
	N		Normal Metabolizer	
	A		Reduced Metabolizer	Consider a reduced warfarin starting dose (3 to 4 mg/day). Dosing recommendations may need to be modified by other clinical factors (eg, age, weight, concurrent medications, and liver disease). Standard INR monitoring is still required. Level of evidence: **Strong**.This patient's reduced metabolizer status predicts increased warfarin anticoagulant effect.
	A		Poor Metabolizer	Consider a reduced warfarin starting dose (0.5 to 2 mg/day). Dosing recommendations may need to be modified by other clinical factors (eg, age, weight, concurrent medications, and liver disease). Standard INR monitoring is still required. Level of evidence: **Strong**.This patient's poor metabolizer status predicts increased warfarin anticoagulant effect.