Supplemental Table 1. Actionable Problem List Entries and Associated Diplotypes

Problem List Entries/Phenotypes	Associated Diplotypes
TPMT Intermediate Activity	*1/*2, *1/*3A, *1/*3B, *1/*3C, *1/*4
TPMT Possible Intermediate Activity	*1/*8
TPMT Low or Absent Activity	*2/*2, *2/*3A, *2/*3B, *2/*3C, *2/*4, *3A/*3A,*3A/*3B, *3A/*3C, *3A/*4, *3B/*3B, *3B/*3C, *3B/*4, *3C/*3C, *3C/*4, *4/*4
CYP2D6 Ultrarapid Metabolizer	(*1/*1)3N, (*1/*2)3N, (*2/*2)3N, (*2/*2)4N
CYP2D6 Possible Ultrarapid Metabolizer	(*1/*10)3N, (*1/*41)3N, (*2/*10)3N, (*2/*41)3N
CYP2D6 Intermediate Metabolizer	(*7/*7)1N, (*9/*9)1N, (*10/*10)1N, (*17/*17)1N, (*29/*29)1N, (*41/*41)1N, (*45/*45)1N, (*46/*46)1N, (*3/*9)2N, (*3/*10)2N, (*3/*17)2N, (*3/*29)2N, (*3/*41)2N, (*3/*45)2N, (*3/*46)2N, (*4/*10)2N, (*4/*9)2N, (*4/*17)2N, (*4/*29)2N, (*4/*41)2N, (*4/*45)2N, (*4/*46)2N, (*6/*9)2N, (*6/*10)2N, (*6/*17)2N, (*6/*29)2N, (*6/*41)2N, (*6/*45)2N, (*6/*46)2N, (*7/*9)2N, (*7/*10)2N, (*7/*17)2N, (*7/*29)2N, (*7/*41)2N, (*7/*45)2N, (*7/*45)2N, (*9/*16)2N, (*9/*36)2N, (*9/*40)2N, (*9/*42)2N, (*10/*16)2N, (*10/*36)2N, (*10/*40)2N, (*10/*42)2N, (*16/*17)2N, (*16/*29)2N, (*16/*41)2N, (*16/*45)2N, (*16/*46)2N, (*17/*36)2N, (*17/*40)2N, (*17/*42)2N, (*29/*36)2N, (*29/*40)2N, (*29/*42)2N, (*36/*41)2N, (*36/*45)2N, (*36/*46)2N, (*40/*41)2N, (*40/*45)2N, (*40/*46)2N, (42/*46)2N, (*41/*42)2N
CYP2D6 Possible Intermediate Metabolizer	(*4/*9)4N
CYP2D6 Poor Metabolizer	(*5/*5)0N, (*3/*3)1N, (*4/*4)1N, (*6/*6)1N, (*7/*7)1N, (*16/*16)1N, (*36/*36)1N, (*40/*40)1N, (*42/*42)1N, (*3/*3)2N, (*3/*4)2N, (*3/*6)2N, (*3/*7)2N, (*3/*16)2N, (*3/*36)2N, (*3/*40)2N, (*3/*42)2N, (*4/*4)2N, (*4/*6)2N, (*4/*7)2N, (*4/*16)2N, (*4/*36)2N, (*4/*42)2N, (*42/*42)2N, (*40/*40)2N, (*6/*6)2N, (*6/*7)2N, (*6/*16)2N, (*6/*36)2N, (*6/*40)2N, (*7/*7)2N, (*7/*16)2N, (*7/*36)2N, (*7/*40)2N, (*7/*42)2N, (*16/*16)2N, (*16/*36)2N, (*16/*40)2N, (*16/*42)2N, (*36/*36)2N, (*36/*40)2N, (*36/*42)2N, (*4/*40)3N

This table only includes diplotypes we have observed and placed results into the EHR; see the PharmGKB (http://www.pharmgkb.org/) website for Translational Pharmacogenetics Project (TPP) gene tables for a more comprehensive list.

Supplemental Table 2. Clinical Decision Support Pre-Test Alerts* by Gene

Gene	Type of Alert	Clinical decision support language
TPMT	Email alert (no order for TPMT genotype)	[Drug name] was just ordered on [patient name] [MRN] Primary Service: [Insert]. However, a TPMT genotype test does not appear to have been ordered for this patient. Please follow up to be certain a TPMT genotype test is ordered and used to guide thiopurine prescribing. The clinician who ordered the thiopurine received a MILLI alert to prompt a TPMT genotype order. This email is sent to the Clinical Pharmacy On Call email group. If you are following this patient, please follow up to be certain a TPMT genotype test is ordered and used to guide thiopurine prescribing. (The email is also sent to members of the PG4KDS team for tracking purposes).
	On-screen alert (no order for TPMT genotype)	TPMT genotype test is recommended before using a thiopurine (mercaptopurine, thioguanine, and azathioprine). A TPMT genotype test does not appear to have been ordered for this patient.
	Email alert (no result for TPMT genotype)	[Drug name] was just ordered on (patient, MRN, primary service). However, a TPMT genotype test result does not appear to be available for this patient. The clinician who ordered the thiopurine received a MILLI alert to prompt careful review of the TPMT result. This email is sent to the Clinical Pharmacy On Call email group. If you are following this patient, please follow up to be certain that TPMT genotype test results are used to guide thiopurine prescribing. (The email is also sent to members of the PG4KDS team for tracking purposes).
	On-screen alert (no result for TPMT genotype)	A TPMT genotype test is recommended before prescribing a thiopurine (mercaptopurine, thioguanine, and azathioprine). A TPMT genotype test was ordered but the result does not appear to be available for this patient. Please contact a clinical pharmacist for help in obtaining TPMT genotype results as soon as possible to guide thiopurine prescribing for this patient.
CYP2D6	Email alert (no order for CYP2D6 genotype)	[Drug name] was just ordered on [patient name] [MRN] Primary Service: [Insert]. There appears to have been no previous CYP2D6 orders on this patient in the past.

* The medications that prompted alerts if a TPMT test result was not in the EHR include azathioprine, mercaptopurine, thioguanine; the medications that prompted a alerts if a CYP2D6 test was not in the EHR included codeine, tramadol, amitriptyline, paroxetine, and fluoxetine.

Supplemental Table 3. Clinical Decision Post-Test Alerts by Problem List Entry for Thiopurines

Medication	Problem List Entry	Post-test Clinical Decision Support Language
Mercaptopurine	TPMT Intermediate Activity	Based on the genotype result, this patient is predicted to have intermediate TPMT activity. The patient is at risk for myelosuppression with normal doses of 6-mercaptopurine. Consider starting 6-mercaptopurine doses at 30 - 70% of the normal dose. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	TPMT Possible Intermediate Activity	This patient either has a mismatch between TPMT genotype and phenotype, or the patient carries a TPMT allele that is not fully characterized. For both situations, this patient MAY have intermediate TPMT activity. If so, the patient would be at increased risk for myelosuppression with normal doses of 6-mercaptopurine. Consider starting 6-mercaptopurine doses at 30-70% of the normal dose and monitoring closely for adverse effects before increasing the dose. Please refer to the pharmacogenetics consult, or TPMT phenotype and/or the thiopurine metabolite consult for more information.
	TPMT Low or absent activity	Based on the genotype result, this patient is predicted to have low or absent TPMT activity. The patient is at high risk for life-threatening myelosuppression with normal doses of 6-mercaptopurine and should receive greatly reduced doses. Start with reducing the normal dose for 6-mercaptopurine by 10-fold and administer thrice weekly instead of daily. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
Azathioprine	TPMT Intermediate Activity	Based on the genotype result, this patient is predicted to have intermediate TPMT activity. The patient is at risk for myelosuppression with normal doses of azaTHIOprine. A normal dose of azaTHIOprine (e.g., 2 - 3 mg/kg/day) should be reduced to 0.6 - 2 mg/kg/day. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	TPMT Possible Intermediate Activity	This patient either has a mismatch between TPMT genotype and phenotype, or the patient carries a TPMT allele that is not fully characterized. For both situations, this patient MAY have intermediate TPMT activity. If so, the patient would be at increased risk for myelosuppression with normal doses of azaTHIOprine. Consider starting azaTHIOprine at 30-70% of the normal dose and monitor closely for adverse effects before increasing the dose. Please refer to the pharmacogenetics consult, or TPMT phenotype and/or the thiopurine metabolite consult for more information.
	TPMT Low or absent activity	Based on the genotype result, this patient is predicted to have low or absent TPMT activity. The patient is at a high risk for life-threatening myelosuppression with normal doses of azaTHIOprine. azaTHIOprine should be avoided, or if azaTHIOprine is given, start by reducing the dose by 10-fold and administer thrice weekly instead of daily. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
Thioguanine	TPMT Intermediate Activity	Based on the genotype result, this patient is predicted to have intermediate TPMT activity. The patient is at risk for myelosuppression with normal doses of thioguanine. Consider an alternative agent or starting thioguanine doses at 30 to 50% of the normal dose. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	TPMT Possible Intermediate Activity	This patient either has a mismatch between TPMT genotype and phenotype, or the patient carries a TPMT allele that is not fully characterized. For both situations, this patient MAY have intermediate TPMT activity. If so, the patient would be at increased risk for myelosuppression with normal doses of thioguanine. Consider starting thioguanine doses at 30-50% of the normal dose and monitoring closely for adverse effects before increasing the dose. Please refer to the pharmacogenetics consult, or TPMT phenotype and/or the thiopurine metabolite consult for more information.
	TPMT Low or absent activity	Thioguanine: Based on the genotype result, this patient is predicted to have low or absent TPMT activity. The patient is at a high risk for life-threatening myelosuppression with normal doses of thioguanine. Consider an alternative agent or reducing the normal dose for thioguanine by 10-fold and administer thrice weekly instead of daily. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.

Supplemental Table 4. Clinical Decision Post-Test Alerts by Problem List Entry for Analgesics Codeine and Tramadol

Medication	Problem List Entry	Post-test Clinical Decision Support Language
Codeine	CYP2D6 Poor Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 poor metabolizer. If codeine is prescribed to a CYP2D6 poor metabolizer, suboptimal analgesia is likely. Other pain medications or cough suppressants are recommended. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Poor Metabolizer	Based on the genotype result, this patient MAY be a CYP2D6 poor metabolizer, although the result is not definitive. If codeine is prescribed to a CYP2D6 poor metabolizer, suboptimal analgesia is likely. Other pain medications or cough suppressants are recommended. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Ultrarapid Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 ultra-rapid metabolizer. If codeine is prescribed to a CYP2D6 ultra-rapid metabolizer, adverse events are likely due to greater conversion to morphine. Other pain medications or cough suppressants are recommended. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Ultrarapid Metabolizer	Based on the genotype result this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. If codeine is prescribed to a CYP2D6 ultra-rapid metabolizer, adverse events are likely due to greater conversion to morphine. Other pain medications or cough suppressants are recommended. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
Tramadol	CYP2D6 Poor Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 poor metabolizer. If traMADol is prescribed to a CYP2D6 poor metabolizer, suboptimal analgesia is likely. Other pain medications are recommended. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Poor Metabolizer	Based on the genotype result, this patient MAY be a CYP2D6 poor metabolizer, although the result is not definitive. If traMADol is prescribed to a CYP2D6 poor metabolizer, suboptimal analgesia is likely. Other pain medications are recommended. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Ultrarapid Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 ultra-rapid metabolizer. If traMADol is prescribed to a CYP2D6 ultra-rapid metabolizer, adverse events are likely due to greater conversion to O-desmethyltramadol. Other pain medications are recommended. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Ultrarapid Metabolizer	Based on the genotype result this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. If traMADol is prescribed to a CYP2D6 ultra-rapid metabolizer, adverse events are likely due to greater conversion to O-desmethyltramadol. Other pain medications are recommended. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.

Supplemental Table 5. Clinical Decision Post-Test Alerts by Problem List Entry for Antidepressants Fluoxetine and Paroxetine

Medication	Problem List Entry	Post-test Clinical Decision Support Language
Fluoxetine	CYP2D6 Poor Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 poor metabolizer. If fluoxetine is prescribed to a CYP2D6 poor metabolizer, plasma levels of fluoxetine are likely to be high, and adverse events are probable. When compared to a CYP2D6 extensive metabolizer, a poor metabolizer may require a 50% dose reduction. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Poor Metabolizer	Based on the genotype result, this patient MAY be a CYP2D6 poor metabolizer. If fluoxetine is prescribed to a CYP2D6 poor metabolizer, plasma levels of fluoxetine are likely to be high, and adverse events are probable. When compared to a CYP2D6 extensive metabolizer, a poor metabolizer may require a 50% dose reduction. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Ultrarapid Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 ultra-rapid metabolizer. If fluoxetine is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of fluoxetine are likely. Other agents not metabolized by CYP2D6 should be considered. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Ultrarapid Metabolizer	Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer. If fluoxetine is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of fluoxetine are likely. Other agents not metabolized by CYP2D6 should be considered. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
Paroxetine	CYP2D6 Poor Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 poor metabolizer. If paroxetine is prescribed to a CYP2D6 poor metabolizer, plasma levels of paroxetine are likely to be high, and adverse events are probable. When compared to a CYP2D6 extensive metabolizer, a poor metabolizer may require a 50% to 75% dose reduction. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Poor Metabolizer	Based on the genotype result, this patient MAY be a CYP2D6 poor metabolizer. If paroxetine is prescribed to a CYP2D6 poor metabolizer, plasma levels of paroxetine are likely to be high, and adverse events are probable. When compared to a CYP2D6 extensive metabolizer, a poor metabolizer may require a 50% to 75% dose reduction. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Ultrarapid Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 ultra-rapid metabolizer. If paroxetine is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. Other agents not metabolized by CYP2D6 should be considered. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Ultrarapid Metabolizer	Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer. If paroxetine is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. Other agents not metabolized by CYP2D6 should be considered. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.

Supplemental Table 6. Clinical Decision Post-Test Alerts by Problem List Entry for Amitriptyline

Medication	Problem List Entry	Post-test Clinical Decision Support Language
Amitriptyline	CYP2D6 Poor Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 poor metabolizer. Amitriptyline has a wide range of dosing recommendations extending from 0.1 to 3 mg/kg/day. If amitriptyline is prescribed at higher doses to a CYP2D6 poor metabolizer, plasma levels of amitriptyline and its active metabolite nortriptyline are likely to be high, and adverse events are probable. When prescribing a higher dose, it is recommended to consider other agents not metabolized by CYP2D6 or reduce the dose and measure plasma levels of the drug and its metabolite nortriptyline. When compared to a CYP2D6 extensive metabolizer, a poor metabolizer may require a 50% dose reduction. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Poor Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 poor metabolizer. Amitriptyline has a wide range of dosing recommendations extending from 0.1 to 3 mg/kg/day. If amitriptyline is prescribed at higher doses to a CYP2D6 poor metabolizer, plasma levels of amitriptyline and its active metabolite nortriptyline are likely to be high, and adverse events are probable. When prescribing a higher dose, it is recommended to consider other agents not metabolized by CYP2D6 or reduce the dose and measure plasma levels of the drug and its metabolite nortriptyline. When compared to a CYP2D6 extensive metabolizer, a poor metabolizer may require a 50% dose reduction. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Ultrarapid Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 ultra-rapid metabolizer. If amitriptyline is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug and its active metabolite are likely. Other agents not metabolized by CYP2D6 should be considered. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Ultrarapid Metabolizer	Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer. If amitriptyline is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug and its active metabolite are likely. Other agents not metabolized by CYP2D6 should be considered. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Intermediate Metabolizer	Based on the genotype result, this patient is predicted to be a CYP2D6 intermediate metabolizer. Amitriptyline has a wide range of dosing recommendations extending from 0.1 to 3 mg/kg/day. If amitriptyline is prescribed at higher doses to a CYP2D6 intermediate metabolizer, plasma levels of amitriptyline and its active metabolite nortriptyline may be high, and adverse events are possible. For treatment of conditions that require a higher dose, it is recommended to consider a dose reduction and measure plasma levels of the drug and its metabolite nortriptyline. When compared to a CYP2D6 extensive metabolizer, an intermediate metabolizer may require a 25% dose reduction. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
	CYP2D6 Possible Intermediate Metabolizer	Based on the genotype result, this patient MAY be a CYP2D6 intermediate metabolizer. Amitriptyline has a wide range of dosing recommendations extending from 0.1 to 3 mg/kg/day. If amitriptyline is prescribed at higher doses to a CYP2D6 intermediate metabolizer, plasma levels of amitriptyline and its active metabolite nortriptyline may be high, and adverse events are possible. For treatment of conditions that require a higher dose, it is recommended to consider a dose reduction and measure plasma levels of the drug and its metabolite nortriptyline. When compared to CYP2D6 extensive metabolizer, an intermediate mediate metabolizer may require a 25% dose reduction. Please consult a clinical pharmacist to review the pharmacogenetics tab for more information.