

The information below can help you understand and apply the results of the Tamoxitest (CYP2D6) Tamoxifen Resistance Test currently offered by Genelex.

Testing for Cytochrome P450 2D6 (CYP2D6) places individuals in one of four categories:

- **Normal Metabolizers (NM)** represent the norm for metabolic capacity. Genotypes consistent with the EM phenotype include two active forms of the gene producing the drug metabolizing enzyme and therefore possess the full complement of drug metabolizing capacity. Generally, extensive metabolizers can be administered drugs which are substrates of the enzyme following standard dosing practices.
- **Intermediate Metabolizers (IM)** may require lower than average drug dosages for optimal therapeutic response for the majority of medications, prodrugs such as tamoxifen may require higher doses. In addition, multiple drug therapy should be monitored closely. Genotypes consistent with the IM phenotype are those with only one active form of the gene producing the drug metabolizing enzyme and therefore have reduced metabolic capacity.
- **Poor Metabolizers (PM)** are at high risk of therapeutic failure because they have a compromised ability to generate the active form of tamoxifen. For the majority of CYP2D6 substrates that are not prodrugs, patients are at increased risk of drug-induced side effects due to diminished drug elimination. Genotypes consistent with the PM phenotype are those with no active genes producing the drug metabolizing enzyme. These individuals have a deficiency in drug metabolism.
- **Ultra-extensive Metabolizers (UM)** may require an increased dosage due to higher than normal rates of drug metabolism for the majority of medications, prodrugs such as tamoxifen may require lower doses. Genotypes consistent with UM phenotype include three or more active genes producing the drug metabolizing enzyme and therefore have increased metabolic capacity.

Although testing is important for tamoxifen, CYP2D6 is responsible for the metabolism of approximately one quarter of medications. If the patient has a variant genotype, please explain that the result will never change in their lifetime and that healthcare providers need to be made aware of the test results. Please refer to the included CYP2D6 substrate list for other common medications metabolized by CYP2D6. A brief presentation is available at www.GeneMedRx.com/explainreport.ppt that further explains results.

Tamoxifen Therapy Modification

Phenotype prevalence is 10 % PM, 7% UM, and 35% IM.

PM – Consider an alternative medication

IM – Consider an alternative medication or an increased dose and avoid multiple drug therapy that inhibits 2D6.

UM- Consider a reduced dose and avoid multiple drug therapy that inhibits 2D6.

EM – Follow standard dosing practices. Avoid multiple drug therapy that inhibits 2D6.

Inhibitors of Cytochrome P-450 2D6

Inhibitors refer to drugs that reduce the ability of the pathway to process drugs. Co-administration will decrease conversion of tamoxifen to the active metabolite endoxifen increasing the possibility of treatment failure. Genelex has included 90-days access to GeneMedRx drug and gene interaction software with the test so healthcare providers can see if any co-administered medications are inhibiting CYP2D6. Here is an abridged list of inhibitors.

amiodarone	chlorpromazine	doxorubicin	methadone	nevirapine	ranitidine	ticlopidine
azelastine	cimetidine	haloperidol	metoclopramide	nicardipine	ritonavir	trifluoperidol
celecoxib	cisapride	indinavir	moclobemide	paroxetine	saquinavir	
chlorpheniramine	cocaine	levomepromazine	nelfinavir	quinidine	terfenadine	

Technical Bulletin

A technical bulletin with more comprehensive information on Cytochrome P450 2D6 is available on our web site at <http://www.healthanddna.com/healthcare-professional/p450-2d6-genotyping.html>.

For immediate consultation Call 877-431-4362

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