



## Tamoxifen PredictAR

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### TAMOXIFEN PredictAR DETERMINES A PATIENT'S CYP2D6 GENOTYPE.

**This knowledge can help  
clinicians predict their patient's  
response to Tamoxifen.**

- 15-20% of women with breast cancer may not receive the full medical benefit from taking Tamoxifen, because of their unique genetic make-up<sup>1</sup>.
- Women with CYP450 (CYP) 2D6 gene variants experience significantly more recurrence of their disease, shorter relapse-free time, and shorter event-free survival rates.<sup>2</sup>
- Selective serotonin reuptake inhibitors (SSRI's), such as paroxetine, that inhibit CYP2D6 can prevent Tamoxifen from being activated.<sup>3</sup>

CYP2D6 may be a marker that identifies patients who will most likely derive benefit from Tamoxifen therapy.

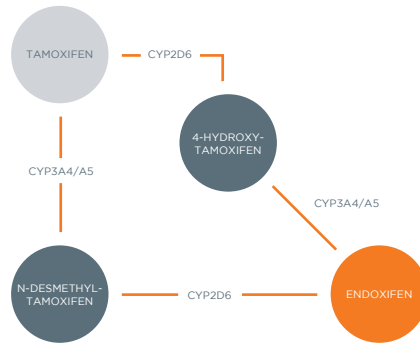
Tamoxifen can be considered a prodrug that requires metabolism to elicit its pharmacological activity. Evidence now suggests that endoxifen, a secondary metabolite of Tamoxifen, is mostly responsible for Tamoxifen activity. In fact, endoxifen is one hundred times more potent as an anti-oestrogen than Tamoxifen itself.

CYP2D6 is the main enzyme that metabolises Tamoxifen to endoxifen. A number of commonly occurring gene variants have been identified in the CYP2D6 gene that result in clinically important changes to CYP2D6 enzyme activity.

Approximately 10% of the Australian population have gene variants in their CYP2D6 gene that results in little or no enzyme activity. These individuals are known as poor metabolisers. As such, poor metabolisers will not receive the full medical benefit of Tamoxifen therapy since they have little capacity to metabolise Tamoxifen to endoxifen. It has now been documented that CYP2D6 poor metabolisers, treated with Tamoxifen, tend to have a shorter relapse-free time, worse relapse-free survival and significantly more recurrence of their disease.

## TAMOXIFEN AND ANTI-DEPRESSANTS

Anti-depressants, in particular selective serotonin reuptake inhibitors (SSRIs), may be commonly prescribed to individuals with breast cancer. However, the choice of SSRI used may have a significant impact on the metabolism of Tamoxifen to endoxifen. This is because some SSRIs (for example, paroxetine) are powerful inhibitors of the CYP2D6 enzyme.



For breast cancer patients, identification of their CYP2D6 genotype may identify those who are less likely to benefit from Tamoxifen therapy.

CYP2D6 poor metabolisers will not receive the full benefit of Tamoxifen, and may be suited to an alternative hormonal therapy.

**Test Name:** Tamoxifen PredictAR

**Sample Type:** 4ml Whole Blood EDTA

**Frequency:** Daily (Mon-Fri)

## REFERENCES

1. Schroth W, Antoniadou L, Fritz P et al: Breast Cancer Treatment Outcome with Adjuvant Tamoxifen Relative to Patient CYP2D6 and CYP2C19 Genotypes. J Clin Oncol 2007; 25: 5187-5193
2. Goetz M.P, Knox S.K, Suman V.J et al: The Impact of Cytochrome P450 2D6 Metabolism in Women Receiving Adjuvant Tamoxifen. Breast Cancer Res Treat 2007; 101: 113-121
3. Borges S, Desta Z, Li L et al: Quantitative Effect of CYP2D6 Genotype and Inhibitors on Tamoxifen Metabolism: Implication for Optimization of Breast Cancer Treatment. Clin Pharmacol Ther 2006; 80: 61-74
4. Schroth W et al. Association Between CYP2D6 Polymorphisms and Outcomes Among Women With Early Stage Breast Cancer Treated With Tamoxifen. JAMA. 2009; 302(13): 1429-1436

All pharmacogenetic test results are interpreted and reported by clinical geneticists at GenesFX Health. The GenesFX Health scientific advisory board comprises clinicians, geneticists, pharmacists and clinical pharmacologists.

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