



Genotype-Guided Tamoxifen Treatment

Policy # 00269

Original Effective Date: 09/15/2010

Current Effective Date: 10/17/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Cytochrome P450 Genotype-Guided Treatment Strategy is addressed separately in medical policy 00169.

Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers genotyping to determine cytochrome p450 2D6 (CYP2D6) variants for the purpose of managing treatment with tamoxifen for women at high risk for or with breast cancer to be **investigational**.*

Background/Overview

TAMOXIFEN METABOLISM

Tamoxifen is a pro-drug that undergoes extensive metabolism to yield its active form: 4-hydroxytamoxifen (4-OH tamoxifen) and 4-hydroxy-N-desmethyltamoxifen (endoxifen). Among these 2 metabolites, endoxifen is thought to be the major metabolite that exerts the pharmacodynamic effect of tamoxifen. The metabolism of tamoxifen into 4-OH tamoxifen is catalyzed by multiple enzymes while endoxifen is formed predominantly by the CYP2D6 enzyme. Plasma concentrations of endoxifen exhibit high interindividual variability, as described in breast cancer patients. Because CYP2D6 enzyme activity is known to vary across individuals, variants in the CYP2D6 gene are of great interest for understanding tamoxifen metabolism variability and variation in levels of circulating active metabolites. Moreover, known variability in endoxifen levels has been hypothesized to result in variable response to tamoxifen treatment.

Metabolic Enzyme Genotypes

The CYP2D6 gene exhibits a high degree of polymorphism, with more than 100 allelic variants identified. The relations among genotype, phenotype, and clinical implications are summarized in Table 1.

Table 1. Relation Among the CYP2D6 Genotype, Phenotype, and Clinical Implications

Genotype	Phenotype	Potential Clinical Implications With Use of Tamoxifen
≥3 copies of functional alleles	Ultrarapid metabolizer	None
Any one of the following scenarios: • 1 active allele and 1 inactive allele • 2 decreased activity alleles • 1 decreased activity allele and 1 inactive allele	Intermediate metabolizer	<ul style="list-style-type: none"> • Increased risk for relapse of breast cancer • Avoid concomitant use of CYP2D6 inhibitors • Consider aromatase inhibitor for postmenopausal women
2 inactive alleles	Poor metabolizer	<ul style="list-style-type: none"> • Increased risk for relapse of breast cancer • Consider aromatase inhibitor for

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

Genotype-Guided Tamoxifen Treatment

Policy # 00269

Original Effective Date: 09/15/2010

Current Effective Date: 10/17/2018

postmenopausal women

Adapted from Swen et al (2011).

The prevalence of *CYP2D6* poor metabolizers is approximately 7% to 10% in whites of Northern European descent, 1.9% to 7.3% in blacks, and 1% or less in most Asian populations studied. The poor metabolizer phenotype in whites is largely accounted for by *CYP2D6**3 and *4 nonfunctional variants, and in black and Asian populations, by the *5 nonfunctional variant. Some poor metabolizers may have 1 nonfunctional allele and 1 reduced-function allele. Among reduced-function variants, *CYP2D6**17, *10, and *8 are the most important in blacks, Asians, and whites, respectively. Few studies have investigated the frequency of *CYP2D6*-variant alleles or poor metabolizers in the Hispanic population.

Endocrine Therapy Regimens

Tamoxifen has several labeled indications:

- chemoprevention of invasive breast cancer in high-risk women without current disease or with ductal carcinoma in situ;
- adjuvant treatment of primary breast cancer; and
- treatment of metastatic disease.

In women with breast cancer, endocrine receptor–positive disease predicts a likely benefit from tamoxifen treatment. Tamoxifen is currently the most commonly prescribed adjuvant treatment to prevent recurrence of the endocrine receptor–positive breast cancer in pre- or perimenopausal women.

For postmenopausal women with osteoporosis or at high-risk for invasive breast cancer, raloxifene is an alternative treatment for invasive cancer risk reduction. Currently, raloxifene is indicated for the treatment of reduction in the “risk of invasive breast cancer in postmenopausal women with osteoporosis” or those at “high risk for invasive breast cancer.”

PHARMACOLOGIC INHIBITORS OF METABOLIC ENZYMES

CYP2D6 activity may be affected not only by genotype but also by coadministered drugs that block or induce *CYP2D6* function. Studies of selective serotonin reuptake inhibitors, in particular, have shown that fluoxetine and paroxetine, but not sertraline, fluvoxamine, or venlafaxine, are potent *CYP2D6* inhibitors. Some individuals treated with fluoxetine or paroxetine have changed from extensive metabolizer phenotype to poor metabolizer. The degree of inhibition may depend on selective serotonin reuptake inhibitors dose.

Thus, *CYP2D6* inhibitor use must be considered in assigning *CYP2D6* functional status, and potent *CYP2D6* inhibitors may need to be avoided when tamoxifen is administered.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. *CYP2D6* genotyping assays are available under the auspices of Clinical

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

Genotype-Guided Tamoxifen Treatment

Policy # 00269

Original Effective Date: 09/15/2010

Current Effective Date: 10/17/2018

Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. FDA has chosen not to require any regulatory review of this test.

Several testing kits for *CYP450* genotyping cleared for marketing by FDA through the 510(k) process (FDA product code: NTI) are summarized in Table 2.

Table 2. Testing Kits for *CYP450* Genotyping Cleared for Marketing by FDA

Device Name	Manufacturer	Approval Date
xTAG CYP2D6 Kit V3	Luminex Molecular Diagnostics	2017
xTAG CYP2C19 Kit V3	Luminex Molecular Diagnostics	2013
Spartan RX CYP2C19 Test System	Spartan Bioscience	2013
xTAG CYP2D6 Kit V3 (including TDAS CYP2D6)	Luminex Molecular Diagnostics	2013
Verigene CYP2C19 Nucleic Acid Test (CYP2C19)	Nanosphere	2012
Infiniti CYP2C19 Assay	AutoGenomics	2010
xTAG CYP2D6 Kit V3, Model I030C0300	Luminex Molecular Diagnostics	2010
Invader UGT1A1 Molecular Assay	Third Wave Technologies	2005
Roche AmpliChip CYP450 Test	Roche Molecular Systems	2005

FDA: Food and Drug Administration.

Several manufacturers market diagnostic genotyping panel tests for *CYP450* genes, such as the YouScript Panel (Genelex Corp.), which includes *CYP2D6*, *CYP2C19*, *CYP2C9*, *VKORC1*, *CYP3A4*, and *CYP3A5*. Other panel tests include both *CYP450* and other non-*CYP450* genes involved in drug metabolism, such as the GeneSight Psychotropic panel (Assurex Health) and PersonaGene Genetic Panels (AlBioTech). These panel tests are beyond the scope of this evidence review.

Centers for Medicare and Medicaid Services (CMS)

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Rationale/Source

The primary goal of pharmacogenomics testing and personalized medicine is to achieve better clinical outcomes in compared with the standard of care. Drug response varies greatly between individuals, and genetic factors are known to play a role. However, in most cases, the genetic variation only explains a modest portion of the variance in the individual response because clinical outcomes are also affected by a wide variety of factors including alternate pathways of metabolism and patient- and disease-related factors that may affect absorption, distribution, and elimination of the drug. Therefore, assessment of clinical utility cannot be made by a chain of evidence from clinical validity data alone. In such cases, evidence evaluation requires studies that directly demonstrate that the pharmacogenomic test alters clinical outcomes; it is not sufficient to demonstrate that the test predicts a disorder or a phenotype.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

Genotype-Guided Tamoxifen Treatment

Policy # 00269

Original Effective Date: 09/15/2010

Current Effective Date: 10/17/2018

function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, two domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

GENOTYPE-GUIDED TAMOXIFEN TREATMENT

Clinical Context and Therapy Purpose

The purpose of genotype-guided tamoxifen treatment is to tailor drug selection (e.g., tamoxifen or an aromatase inhibitor) or dose selection (e.g., tamoxifen 40 mg/d instead of the standard 20 mg/d dose) or strategy (e.g., ovarian ablation in premenopausal women) while minimizing treatment failures or toxicities based on a patient's genotype.

The question addressed in this evidence review is: Does a genotyping-guided treatment strategy change patient management in a way that it improves net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is patients receiving or being considered for tamoxifen therapy:

- Treatment of breast cancer in the adjuvant setting to prevent recurrence (alone or preceding aromatase inhibitor therapy) or for metastatic disease.
- Prevention of breast cancer in high-risk women or women with ductal carcinoma in situ; and absence of contraindications to aromatase inhibitors (for treatment) or raloxifene (for disease prevention).

Interventions

The test being considered is *CYP2D6* genotype-guided tamoxifen treatment. Commercial tests for individual genes or gene panels are available and listed in the Regulatory Status section.

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

Genotype-Guided Tamoxifen Treatment

Policy # 00269

Original Effective Date: 09/15/2010

Current Effective Date: 10/17/2018

Comparators

The following practice is currently being used: clinically managed tamoxifen treatment.

Outcomes

The general outcomes of interest are overall survival, disease-specific survival, medication use, and treatment-related morbidity. Specific outcomes are listed in Table 3.

Table 3. Outcomes of Interest for Individuals With or at High Risk for Breast Cancer

Outcomes	Details
Medication use	Change to alternative treatment (aromatase inhibitor) or strategy (ovarian ablation in premenopausal women)
Treatment-related morbidity	Reduction in adverse events

The potential beneficial outcomes of primary interest would be a reduction in the rate of recurrence and improvement in disease-free survival or overall survival.

Timing

Follow-up to determine whether genotype-guided tamoxifen treatment reduces adverse events or avoids treatment failure is during the first 10 years after treatment initiation.

Setting

Patients requiring treatment for prevention or treatment for breast cancer are managed by an oncologist.

Prospective Cohort Studies

Multiple retrospective and prospective cohort studies have investigated the association between *CYP2D6* genotype and tamoxifen effectiveness and reported contradictory results with relative risks ranging from 0.08 to 13.1 for the association between variant *CYP2D6* genotypes and breast cancer recurrence or mortality. The contradictory results may be due to differences in the types of additional therapies patients received, how many and which *CYP2D6* alleles were tested, tissue type examined (tumor or germline deoxyribonucleic acid [DNA]), and coadministration with *CYP2D6* inhibitors. Many of these studies have also been summarized in multiple systematic reviews and meta-analyses with inconsistent results. Data in most of these studies derived from a convenient sample, which was further limited by relatively small numbers of patients, lack of comprehensive genotype data and patient data (e.g., concomitant medications), and detailed clinical outcomes data. Among the most influential studies of the association between *CYP2D6* genotype and tamoxifen effectiveness are 3 nonconcurrent prospective studies nested within large prospective, randomized double-blind trials that compared tamoxifen with anastrozole, letrozole, or combination tamoxifen and anastrozole in postmenopausal women with hormone receptor-positive early-stage breast cancer. In the Arimidex, Tamoxifen, Alone or in Combination (ATAC) trial and Breast International Group 1-98 (BIG 1-98) trial, a subset of patients who received tamoxifen and were genotyped for *CYP2D6* variants (n=588 and n=1243, respectively) did not show any statistically significant associations between phenotype (patients classified as poor, intermediate, or extensive metabolizer) and

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

Genotype-Guided Tamoxifen Treatment

Policy # 00269

Original Effective Date: 09/15/2010

Current Effective Date: 10/17/2018

breast cancer recurrence. In the Austrian Breast and Colorectal Cancer Study Group trial, a case-control study was done using a subset of patients where cases were defined as those with disease recurrence, contralateral breast cancer, second non-breast cancer, or died and controls were identified from the same treatment arm of similar age, surgery/radiation, and stage. Results showed that patients with 2 poor metabolizer alleles had higher likelihood of recurrence than women with 2 extensive metabolizer alleles. Concerns about the substantial departure from Hardy-Weinberg equilibrium for the *CYP2D6* allele, *4 and analyses not meeting the Simon-Paik-Hayes criteria for nonconcurrent prospective studies have been raised to explain the lack of effect in the ATAC and BIG 1-98 trials.

Trials are important to validate such hypotheses. However, no trials of genotype-directed dosing or drug choice that assessed outcomes of breast cancer recurrence were identified. Ruddy et al (2013) implemented a tamoxifen adjustment algorithm for 99 patients treated at a cancer treatment institute. Recommendations to modify tamoxifen therapy were made for 18 (18%) patients, all of whom had low endoxifen levels (<6 ng/mL), and 2 of whom also were identified as *CYP2D6* poor metabolizers. Breast cancer recurrence or survival outcomes were not reported.

SUMMARY OF EVIDENCE

For individuals who are treated with tamoxifen for breast cancer or are high risk for breast cancer who receive *CYP2D6* genotype-guided tamoxifen treatment, the evidence includes multiple retrospective and prospective cohort studies and nonconcurrent prospective studies. Relevant outcomes include overall survival, disease-specific survival, medication use, and treatment-related morbidity. Published data on the association between *CYP2D6* genotype and tamoxifen treatment outcomes have yielded inconsistent results. Data in most of these studies derived from a convenient sample, which was further limited by relatively small numbers of patients and lack of comprehensive genotype data, patient data (e.g., concomitant medications), and detailed clinical outcomes data. Three influential nonconcurrent prospective studies nested within large prospective, randomized double-blind clinical trials in postmenopausal women with hormone receptor-positive early-stage breast cancer also reported contradictory results, with 2 larger studies failing to show statistically significant associations between phenotype (patients classified as poor, intermediate, or extensive metabolizer) and recurrence of breast cancer. No trials of genotype-directed dosing or drug choice that compared health outcomes for patients managed with and without the test were identified. It is not known whether *CYP2D6* genotype-guided tamoxifen treatment results in the selection of a treatment strategy that would reduce the rate of breast cancer recurrence, improve disease-free survival or overall survival, or reduce adverse events. The evidence is insufficient to determine the effects of the technology on health outcomes.

References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, "Genotype-Guided Tamoxifen Treatment", 2.04.51, 7:2018.
2. Goetz MP, Kamal A, Ames MM. Tamoxifen pharmacogenomics: the role of CYP2D6 as a predictor of drug response. *Clin Pharmacol Ther*. Jan 2008;83(1):160-166. PMID 17882159
3. Stearns V, Johnson MD, Rae JM, et al. Active tamoxifen metabolite plasma concentrations after coadministration of tamoxifen and the selective serotonin reuptake inhibitor paroxetine. *J Natl Cancer Inst*. Dec 3 2003;95(23):1758-1764. PMID 14652237

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

Genotype-Guided Tamoxifen Treatment

Policy # 00269

Original Effective Date: 09/15/2010

Current Effective Date: 10/17/2018

4. Swen JJ, Nijenhuis M, de Boer A, et al. Pharmacogenetics: from bench to byte--an update of guidelines. *Clin Pharmacol Ther.* May 2011;89(5):662-673. PMID 21412232
5. Bernard S, Neville KA, Nguyen AT, et al. Interethnic differences in genetic polymorphisms of CYP2D6 in the U.S. population: clinical implications. *Oncologist.* Feb 2006;11(2):126-135. PMID 16476833
6. Drugs.com. Tamoxifen. 2017; https://www.drugs.com/pro/tamoxifen.html#ID_5d3c080c-ceac-4255-ae0f0-9ce46bd1c916. Accessed June 27, 2018.
7. Eli Lilly. Highlights from Prescribing Information: Evista (raloxifene hydrochloride) tablet for oral use. 2016; <http://pi.lilly.com/us/evista-pi.pdf>. Accessed June 27, 2018.
8. Alfaro CL, Lam YW, Simpson J, et al. CYP2D6 status of extensive metabolizers after multiple-dose fluoxetine, fluvoxamine, paroxetine, or sertraline. *J Clin Psychopharmacol.* Apr 1999;19(2):155-163. PMID 10211917
9. Alfaro CL, Lam YW, Simpson J, et al. CYP2D6 inhibition by fluoxetine, paroxetine, sertraline, and venlafaxine in a crossover study: intraindividual variability and plasma concentration correlations. *J Clin Pharmacol.* Jan 2000;40(1):58-66. PMID 10631623
10. Lam YW, Gaedigk A, Ereshefsky L, et al. CYP2D6 inhibition by selective serotonin reuptake inhibitors: analysis of achievable steady-state plasma concentrations and the effect of ultrarapid metabolism at CYP2D6. *Pharmacotherapy.* Aug 2002;22(8):1001-1006. PMID 12173784
11. Ahern TP, Hertz DL, Damkier P, et al. Cytochrome P-450 2D6 (CYP2D6) genotype and breast cancer recurrence in tamoxifen-treated patients: evaluating the importance of loss of heterozygosity. *Am J Epidemiol.* Jan 15 2017;185(2):75-85. PMID 27988492
12. Rae JM, Drury S, Hayes DF, et al. CYP2D6 and UGT2B7 genotype and risk of recurrence in tamoxifen-treated breast cancer patients. *J Natl Cancer Inst.* Mar 21 2012;104(6):452-460. PMID 22395643
13. Regan MM, Leyland-Jones B, Bouzyk M, et al. CYP2D6 genotype and tamoxifen response in postmenopausal women with endocrine-responsive breast cancer: the Breast International Group 1-98 trial. *J Natl Cancer Inst.* Mar 21 2012;104(6):441-451. PMID 22395644
14. Goetz MP, Suman VJ, Hoskin TL, et al. CYP2D6 metabolism and patient outcome in the Austrian Breast and Colorectal Cancer Study Group trial (ABCSCG) 8. *Clin Cancer Res.* Jan 15 2013;19(2):500-507. PMID 23213055
15. Goetz MP, Ratain M, Ingle JN. Providing balance in ASCO Clinical Practice Guidelines: CYP2D6 genotyping and tamoxifen efficacy. *J Clin Oncol.* Nov 10 2016;34(32):3944-3945. PMID 27551126
16. Ruddy KJ, Desantis SD, Gelman RS, et al. Personalized medicine in breast cancer: tamoxifen, endoxifen, and CYP2D6 in clinical practice. *Breast Cancer Res Treat.* Oct 2013;141(3):421-427. PMID 24062210
17. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology: breast cancer. Version 1.2018. http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed June 12, 2018.
18. Harris LN, Ismaila N, McShane LM, et al. Use of biomarkers to guide decisions on adjuvant systemic therapy for women with early-stage invasive breast cancer: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol.* Apr 1 2016;34(10):1134-1150. PMID 26858339

Policy History

Original Effective Date: 09/15/2010

Current Effective Date: 10/17/2018

09/09/2010	Medical Policy Committee review
09/15/2010	Medical Policy Implementation Committee approval. New policy.
09/01/2011	Medical Policy Committee review
09/14/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/06/2012	Medical Policy Committee review
09/19/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/23/2013	Coding updated
09/05/2013	Medical Policy Committee review
09/18/2013	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/04/2014	Medical Policy Committee review
09/17/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/03/2015	Medical Policy Committee review
09/23/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

Genotype-Guided Tamoxifen Treatment

Policy # 00269
 Original Effective Date: 09/15/2010
 Current Effective Date: 10/17/2018

09/08/2016 Medical Policy Committee review
 09/21/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
 01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
 09/07/2017 Medical Policy Committee review
 09/20/2017 Medical Policy Implementation Committee approval. Policy revised with updated genetics nomenclature; coverage eligibility otherwise unchanged.
 02/06/2018 Coding update
 10/04/2018 Medical Policy Committee review
 10/17/2018 Medical Policy Implementation Committee approval. Title changed from "Genetic Testing for Tamoxifen Treatment" to "Genotype Guided Tamoxifen Treatment". Coverage eligibility unchanged.
 Next Scheduled Review Date: 10/2019

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2017 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply. CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	81226 Code deleted eff 1/1/18: 0015U Codes added eff 10/1/18: 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U
HCPCS	No codes
ICD-10 Diagnosis	C50.011-C50.019 C50.111-C50.119 C50.211-C50.219 C50.311-C50.319 C50.411-C50.419 C50.511-C50.519 C50.611-C50.619 C50.811-C50.819 C50.911-C50.919

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

Genotype-Guided Tamoxifen Treatment

Policy # 00269

Original Effective Date: 09/15/2010

Current Effective Date: 10/17/2018

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 - 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
 - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 - 3. Reference to federal regulations.

† Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.