Clinical Appropriateness Guidelines

Pharmacogenomic Testing

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AIM SpecialtyHealth
8600 West Bryn Mawr Avenue
South Tower - Suite 800 Chicago, IL 60631
www.aimspecialtyhealth.com

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Scope

Pharmacogenomic testing broadly describes how one's genome, or multiple genes, can influence drug response while more targeted pharmacogenetic testing describes genotyping a specific gene to predict response to certain medications. This document addresses pharmacogenomic testing for the purpose of informing medication selection, dosage, and risk of adverse side effects. This guideline does not address tumor testing (see Clinical Appropriateness Guideline Molecular Testing of Solid and Hematologic Tumors and Malignancies) or germline testing (See Clinical Appropriateness Guideline Genetic Testing for Hereditary Cancer Susceptibility) performed to direct treatment decisions or genetic testing to generate polygenic risk scores (see Clinical Appropriateness Guideline for Genetic Testing for Single-Gene and Multifactorial Conditions). All tests listed in these guidelines may not require prior authorization; please refer to the health plan.

Appropriate Use Criteria

Pharmacogenomic Testing

Pharmacogenetic testing of common variants associated with drug metabolism is medically necessary when either of the following criteria is met:

- All of the following:
  - The individual is a candidate for a targeted drug therapy associated with a specific genotype
  - The results of the pharmacogenetic test will directly impact clinical decision-making and clinical outcome for the individual
  - Published, peer-reviewed studies have proven that identifying the specific genetic variant improves clinical outcomes
- Identification of the genetic variant is required or recommended in a specific population prior to initiating therapy with the target drug as noted by the U.S. Food and Drug Administration (FDA)-approved prescribing label

Multi-gene pharmacogenomic genotyping assays in which each included target does not meet the above criteria are not medically necessary.

Warfarin Administration

Testing of CYP2C9 and/or VKORC1 is medically necessary for individuals being treated with warfarin who have not achieved a stable dose AND either of the following:

- An unusually low maintenance dose of warfarin (<0.5mg)
- An international normalized ratio (INR) >4.0 during standard dosing

CPT Codes

The following codes are associated with the guidelines in the document. This list is not all inclusive. Medical plans may have additional coverage policies that supersede these guidelines.

Covered when medical necessity criteria are met:

81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17)
81226	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)
81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6)
81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7)
81232	DPYD (dihydropyrimidine dehydrogenase) (eg, 5-fluorouracil/5-FU and capecitabine drug metabolism), gene analysis, common variant(s) (eg, *2A, *4, *5, *6)
81306	NUDT15 (nudix hydrolase 15) (eg, drug metabolism) gene analysis, common variant(s) (eg, *2, *3, *4, *5, *6)
81335	TPMT (thiopurine S-methyltransferase) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)
81350	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (eg, drug metabolism, hereditary unconjugated hyperbilirubinemia [Gilbert syndrome]) gene analysis, common variants (eg, *28, *36, *37)
81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (eg, warfarin metabolism), gene analysis, common variant(s) (eg, -1639G>A, c.173+1000C>T)
81381	HLA Class I typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, B*57:01P), each
81404	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (eg, hereditary unconjugated hyperbilirubinemia [Crigler-Najjar syndrome]) full gene sequence
0030U	Drug metabolism (warfarin drug response), targeted sequence analysis (ie, CYP2C9, CYP4F2, VKORC1, rs12777823)
0034U	TPMT (thiopurine S-methyltransferase), NUDT15 (nudix hydroxylase 15) (eg, thiopurine metabolism), gene analysis, common variants (ie, TPMT *2, *3A, *3B, *3C, *4, *5, *6, *8, *12; NUDT15 *3, *4, *5)

0070U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, common and select rare variants (ie, *2, *3, *4, *4N, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14A, *14B, *15, *17, *29, *35, *36, *41, *57, *61, *63, *68, *83, *xN)
0169U	NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (eg, drug metabolism) gene analysis, common variants

Codes that do not meet medical necessity criteria:

81230	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22)
81291	MTHFR (5,10-methylenetetrahydrofolate reductase) (eg, hereditary hypercoagulability) gene analysis, common variants (eg, 677T, 1298C)
81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (eg, adverse drug reaction), gene analysis, common variant(s) (eg, *5)
81346	TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (eg, tandem repeat variant)
0029U	Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis (ie, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, VKORC1 and rs12777823)
0031U	CYP1A2 (cytochrome P450 family 1, subfamily A, member 2) (eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7)
0032U	COMT (catechol-O-methyltransferase) (drug metabolism) gene analysis, c.472G>A (rs4680) variant
0033U	HTR2A (5-hydroxytryptamine receptor 2A), HTR2C (5-hydroxytryptamine receptor 2C) (eg, citalopram metabolism) gene analysis, common variants (ie, HTR2A rs7997012 [c.614-2211T>C], HTR2C rs3813929 [c.- 759C>T] and rs1414334 [c.551-3008C>G])
0071U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, full gene sequence (List separately in addition to code for primary procedure) (Use 0071U in conjunction with 0070U)
0072U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D6-2D7 hybrid gene) (List separately in addition to code for primary procedure) (Use 0072U in conjunction with 0070U)
0073U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, CYP2D7-2D6 hybrid gene) (List separately in addition to code for primary procedure) (Use 0073U in conjunction with 0070U)

0074U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, non-duplicated gene when duplication/multiplication is trans) (List separately in addition to code for primary procedure) (Use 0074U in conjunction with 0070U)
0075U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 5' gene duplication/multiplication) (List separately in addition to code for primary procedure) (Use 0075U in conjunction with 0070U)
0076U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism) gene analysis, targeted sequence analysis (ie, 3' gene duplication/ multiplication) (List separately in addition to code for primary procedure) (Use 0076U in conjunction with 0070U)
0078U	Pain management (opioid-use disorder) genotyping panel, 16 common variants (ie, ABCB1, COMT, DAT1, DBH, DOR, DRD1, DRD2, DRD4, GABA, GAL, HTR2A, HTTLPR, MTHFR, MUOR, OPRK1, OPRM1), buccal swab or other germline tissue sample, algorithm reported as positive or negative risk of opioid-use disorder
0173U	Psychiatry (ie, depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes
0175U	Psychiatry (eg, depression, anxiety), genomic analysis panel, variant analysis of 15 genes
0258U	Autoimmune (psoriasis), mRNA, next generation sequencing, gene expression profiling of 50-100 genes, skin-surface collection using adhesive patch, algorithm reported as likelihood of response to psoriasis biologics
ANY	GeneSight®

Background

Pharmacogenomic Testing

Pharmacogenomic testing is utilized as a tool in the field of precision medicine. Precision medicine can guide optimal health care decisions by identifying individual variability to direct approaches for

prevention, diagnosis, and treatment of disease (Collins and Varums 2015). As this approach to clinical practice has grown, so has the availability of pharmacogenomic testing in the clinical realm.

The CYP450 gene superfamily is composed of many isoenzymes that are involved in the metabolism of about 75% of commonly prescribed drugs. Many of the clinically available pharmacogenomic tests include genes related to the CYP450 superfamily. CYP2C19, CYP2D6 and CYP2C9 enzymes metabolize approximately 15%, 20-25%, and 10% of all currently used drugs, respectively, that are most often prescribed as treatments for oncologic, psychiatric, neurologic, or cardiovascular conditions (Drozda et al. 2014). These genes are highly polymorphic, and certain genotypes have been classified by their effect on metabolism (poor, intermediate, normal or ultrarapid) of specific drugs. While the speed of metabolism can affect optimal dosing strategy for a drug, it is also important to note that genetic variability accounts for only a portion of the individual differences in drug response, and there are many other variables in the pharmacokinetics and pharmacodynamics of medications (Solomon, Cates and Li 2019; Pasternak et al. 2017).

Single Gene Pharmacogenetic Assays

There are many challenges in gathering sufficient evidence to support the clinical utility of pharmacogenetic testing, including the relatively low effect size of individual variants, the complex interactions between different genetic variants and the large number of confounding factors in medication response across individuals. In addition, there is a high degree of variability in study design, methods, and measured outcomes in the published literature, making comparisons difficult (Fabbri et al. 2018; Zeier et al. 2018; Jarvis et al. 2019). Other limitations of published studies include conflicts of interest among the researchers and lack of blinding for participants and providers (Zeier et al. 2018; Bousman and Dunlop 2018). While genotype-guided drug choice or dosing has been shown to increase efficacy and limit side effects for certain medications, the clinical utility of most pharmacogenetic testing has not yet been established.

The US Food and Drug Administration (FDA) includes pharmacogenetic testing recommendations with the labeling of many drugs. In some cases, genetic testing is required to determine if the patient will respond to the planned treatment. For example, certain pharmacologic chaperone molecules are only effective against disease caused by specific types of genetic pathogenic variants (e.g., ivacaftor for cystic fibrosis and migalastat for Fabry disease). Genetic testing is also required when there is a well-established risk that the medication will trigger severe complications in individuals with specific genetic variants, such as rasburicase in individuals with G6PD deficiency and abacavir hypersensitivity in individuals with the HLA-B*57:01 allele. Other FDA labels do not provide a strong recommendation for genetic testing, but note that there may be actionable information about optimal dosing, efficacy, or toxicity of the drug in a subset of patients with a specific genotype. This is often the case for drugs known to interact with the CYP450 genes. In other cases, the FDA will note that a gene is known to be involved in the metabolism or pharmacodynamics of the drug, but there is limited or no evidence of different responses among people with different genotypes, and the clinical utility of testing prior to administration is not clear. The overall number of drugs which have genetic testing requirements on the FDA label is relatively small. Many drug/gene pairs for which testing is mentioned on the FDA label are based on evidence from laboratory studies, case reports, or observational studies rather than randomized controlled trials or large subgroup analyses (Chin et al. 2017). Additional recommendations or guidelines are often needed to help clinicians assess the clinical utility of pharmacogenetic testing. In many cases, there is limited evidence that pharmacogenetic testing results in better clinical outcomes (Dong et al. 2018; Nurnberger et al. 2018). In addition, there is

significant variability in the specific alleles that are evaluated by different clinical tests. This complicates result interpretation, especially in ethnically diverse populations. It is important to interpret results of pharmacogenetic testing with these limitations in mind (Pratt et al. 2018; Pratt et al. 2019).

The Clinical Pharmacogenetics Implementation Consortium (CPIC) have established guidelines to assist clinicians in guiding drug therapy and dosage based on existing pharmacogenetic results. CPIC guidelines are developed in a standard format after rigorous review and grading of the literature and extensive peer review. They are meant to provide guidance for the use of existing genetic test results, but do not provide recommendations about whether to order specific genetic tests (Caudle et al. 2014).

Multi-Gene Pharmacogenomic Assays

While targeted gene testing for variants in some genes has been proposed to predict patient-specific drug metabolism of specific drugs, there still exists a lack of robust evidence to support the clinical utility of panel testing for multiple genes. There are a number of clinically available combined pharmacogenomic panel tests designed to evaluate variants within multiple genes to provide guidance for prescribing and dosing various medications which may ultimately aid in addressing the recognized need to alleviate prolonging or complicating the clinical course of a patient's condition due to side effects or lack of response from a trial-and-error approach to medication choice. These panel tests are even marketed as "decision support tools" (Bousman and Dunlop 2018). While pharmacogenomic tests are a promising candidate to address this need, as evidenced by many retrospective reviews, there is a lack of large and adequately powered randomized controlled studies that address whether the use of pharmacogenomic panels in prescribing medications improves outcomes in various conditions (Drozda et al. 2014; Zeier et al. 2018; Lin and Chun 2019). Another hurdle, as evidenced by the systematic review of available studies by Fabbri et al. (2019), is the lack of best practice guidelines for developing clinical evidence. This deficit ultimately impacts the quality of available studies.

Evidence to support pharmacogenomic-guided antidepressant treatment is generally low strength because randomized controlled trials are few and underpowered, and variability in study designs make direct comparisons difficult (Perterson et al. 2017; Rosenblat and McIntyre 2017; Solomon, Cates and Li 2018). While published results from a recent large patient-blinded randomized controlled trial, the Genomics Used to Improve DEpression Decisions (GUIDED) trial, revealed that patients reached secondary outcomes of improvements in response (26.0% versus 19.9%, p=0.036) and remission (15.3% versus 10.1%, p=0.007) rates compared to patients with treatment as usual; the study failed to meet the primary outcome of statistically significant symptom improvement (27.2% versus 24.4%, p=0.107) in patients with treatment guided by pharmacogenomic testing (Greden et al. 2019). This study adds more data to the literature purporting a promising future for pharmacogenomic-directed treatment, but it also underscores the need for additional evidence to support it beyond paired cytochrome gene testing. In addition, it highlights the conundrum of available market-place genetic tests' rate of evolution outpacing evidence of clinical utility in the newest iteration, i.e., the current pharmacogenomic panel available on the market is larger than the panel studied in the GUIDED trial.

The majority of professional society guidelines related to pharmacogenomic testing address specific drug-gene interactions rather than multi-gene panels (Beckett et al. 2018). Although individual biomarkers may have clinical utility in certain circumstances, clinicians will often choose larger panels due to the increasing availability in the market (Moyer et al. 2017), without sufficient evidence that panel testing of multiple genes has any benefit over single-gene testing or standard trial-and-error methods (Zeier et al. 2018).

Among clinically available pharmacogenomic panel tests, interpretation of results and final medication recommendations vary substantially and even contradict each other, highlighting the need for standardized guidelines before panel-based pharmacogenomic testing becomes a routine part of clinical practice (Bousman and Dunlop 2018; Bousman et al. 2018). In 2018, the FDA issued a consumer warning against the use of many pharmacogenetic tests, indicating that there is limited scientific and clinical evidence to support the claims of clinical utility that are advertised by these laboratories (FDA 2018). Subsequently, the FDA issued a statement in 2020 introducing a web-based resource that includes a table of certain gene-drug interactions the FDA feels sufficient evidence is available to support the association between genetic variants and drug metabolism. The FDA does note this table is not complete, and also does not provide references to support the pharmacogenetic associations included in the table (FDA 2020).

Warfarin Administration

While there are numerous challenges to warfarin dosing with its highly variable individual responses and challenges achieving and maintaining levels within a therapeutic range, it has the potential to significantly reduce morbidity and mortality from thromboembolic events (Flockhart et al. 2008). Many current guidelines remain silent on the use of pharmacogenetics to guide warfarin therapy. The American College of Medical Genetics and Genomics (ACMG) guideline (2008) does not recommend routine use of pharmacogenetic testing for warfarin. However, they do carve out practical scenarios where testing may be beneficial (Flockhart et al. 2008). The guideline specifically notes CYP2C9 and VKORC1 genotypes can reasonably be used as part of diagnostic efforts to determine the cause of an unusually low maintenance dose of warfarin or an unusually high INR during standard dosing (Flockhart et al. 2008). In doing so, health care providers would be able to spend less time and energy on the issues of drug interactions and diet, both of which can be inordinately time consuming in this setting. Testing should not be performed in patients who have achieved a stable dose of warfarin, only in those having difficulty getting to a stable dose upon initiation of warfarin therapy.

Professional Society Guidelines

American College of Medical Genetics and Genomics (ACMG)

ACMG Policy Statement. Pharmacogenetic Testing of CYP2C9 and VKORC1 Alleles for Warfarin.
Flockhart DA, O'Kane D, Williams MS, Watson MS, et al; ACMG Working Group. Genet Med. 2008 Feb;10(2):139-50. PubMed PMID: 18281922.

ACMG Points to Consider Statement. DNA-Based Screening and Population Health.
Murray M, Giovanni M, Doyle D, et al. Genet Med. 2021 Jun;23(6):989-995. PubMed PMID: 33727704.

Association for Molecular Pathology (AMP)

AMP Recommendations for Clinical CYP2C19 Genotyping Allele Selection.
Pratt VM, Del Tredici AL, Hachad H, et al. J Mol Diagn 2018. May;20(3):269-276. Epub 2018 Feb 21. PubMed PMID: 29474986.

AMP Recommendations for Clinical Warfarin Genotyping Allele Selection.
Pratt V, Cavallari L, Tredici A., et al. J Mol Diagn. 2020 Jul;22(7):847-859. PMID: 32380173.

Clinical Pharmacogenetics Implementation Consortium (CPIC)

CPIC Guideline. CYP2C19 Genotype and Clopidogrel Therapy.
Scott SA, Sangkuhl K, Stein CM, et al. Clin Pharmacol Ther. 2013 Sep;94(3):317-23. PubMed PMID: 23698643.

CPIC Guideline. CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants
Hicks JK, Sangkuhl K, Swen JJ, et al. Clin Pharmacol Ther. 2017 Jul 102(1):37-44. PubMed PMID: 27997040.

CPIC Guideline. CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors.
Hicks JK, Bishop JR, Sangkuhl K, et al. Clin Pharmacol Ther. 2015 Aug;98(2):127-34. PubMed PMID: 25974703.

CPIC Guidelines. CYP2C9 and HLA-B Genotype and Phenytoin Dosing. 2020 Update.
Karnes JH, Rettie AE, Somogyi AA, et al. Clin Pharmacol Ther. 2020 Aug 11. Epub ahead of print. PMID: 32779747.

CPIC Guideline. CYP2D6 and Tamoxifen Therapy.
Goetz MP, Sangkuhl K, Guchelaar HJ, et al. Clin Pharmacol Ther. 2018 May;103(5):770-777. PubMed PMID: 29385237.

CPIC Guideline. CYP2D6 Genotype and Use of Ondansetron and Tropisetron.
Bell GC, Caudle KE, Whirl-Carrillo M, et al. Clin Pharmacol Ther. 2017 Aug;102(2):213-18. PubMed PMID: 28002639.

CPIC Guideline. CYP2D6, OPRM1, and COMT Genotype and Select Opioid Therapy.
Crews K, Monte A, Huddart R, et al. Clin Pharmacol Ther. 2021 Jan 2. PubMed PMID: 33387367.

CPIC Guideline. Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing.
Amstutz U, Henricks LM, Offer SM, et al. Clin Pharmacol Ther. 2018 Feb;103(2):210-216. PubMed PMID: 29152729.

CPIC Guideline. HLA Genotype and Use of Carbamazepine and Oxcarbazepine.
Phillips EJ, Sukasem C, Whirl-Carrillo M, et al. Clin Pharmacol Ther. 2018 Apr;103(4):574-581. PubMed PMID: 29392710.

CPIC Guideline. Pharmacogenetics-Guided Warfarin Dosing.
Johnson JA, Caudle KE, Gong L, et al. Clin Pharmacol Ther. 2017 Sep;102(3):397-404. PubMed PMID: 28198005.

CPIC Guideline. Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes.
Relling MV, Schwab M. Whirl-Carrillo M, et al. Clin Pharmacol Ther. 2019 May;105(5):1095-1105. PubMed PMID: 30447069.

Joint Statements

AMP and College of American Pathologists (CAP). Recommendations for Clinical CYP2C9 Genotyping Allele Selection.
Pratt VM, Cavallari LH, Del Tredici AL, et al. J Mol Diagn. 2019 May 7. PubMed PMID: 31075510.

AMP, College of American Pathologists (CAP), Dutch Pharmacogenetics Working Group of the Royal Dutch Pharmacists Association, and European Society for Pharmacogenomics and Personalized Therapy. Recommendations for Clinical CYP2D6 Genotyping Allele Selection.
Pratt VM, Cavallari L, Del Tredici AL, et al. J Mol Diagn. 2021 Jun 10: S1525-1578(21)00164-1. PubMed PMID: 34118403.

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Revision History

Medical Advisory Board Review:

v1.2022 09/20/2021: Approved

v2.2021 03/12/2021: Approved

v1.2021 11/13/2020: Approved

v2.2020 05/08/2020: Reviewed

v1.2020 11/04/2019: Reviewed

v2.2019 05/23/2019: No Criteria Changes

v1.2019 11/07/2018: Reviewed

v1.2018 03/31/2018: Reviewed

Clinical Steering Committee Review:

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v2.2021 02/22/2021: Approved

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Revisions:

Version	Date	Editor	Description
v1.2022 *GEN06-0322.1*	08/16/2021	Carrie Langbo, MS, CGC	Semi-annual review. Genetic testing for Thrombophilia criteria, CPT codes, professional society guidelines and references were moved to the Genetic Testing Guideline for Single Gene and Multifactorial Conditions. The

			Background and Professional Society Guidelines were updated.
v2.2021 *GEN06-0921.1*	02/15/2021	Carrie Langbo, MS, CGC	Semi-annual review. No criteria changes. Professional society guidelines were updated.
v1.2021	9/11/2020	Carrie Langbo, MS, CGC	Semi-annual review. Background, professional society guidelines and references were updated.
v2.2020	03/13/2020	Ann Schmidt, MS, CGC	Semi-annual review. Criteria was expanded to cover testing for CYP2C9 and VKORC1. CPT codes, background and references were updated.
v1.2020	09/11/2019	Carrie Langbo, MS, CGC	Semi-annual review. Criteria was expanded to allow thrombophilia testing in pregnant women with a history of any type of VTE. Revised terminology for pharmacogenomic and pharmacogenetic testing. Updated professional society guidelines, background and references.
v2.2019	04/03/2019	Ann Schmidt, MS, CGC	Semi-annual review. No criteria changes. Updated professional society guidelines and references.
v1.2019	10/03/2018	Kate Charyk, MS, CGC	Semi-annual review. Professional society guidelines and references updated. Renumbered to 2019. Reformatted CPT code list. PMID added.
v1.2018	03/31/2018	Heather Dorsey, MS, CGC	Semi-annual review. Expanded F2/F5 criteria to allow additional management changes for unprovoked VTE and estrogen changes with significant family history. Disclaimer sentence added to scope. Professional society guidelines

			and references updated. Renumbered to 2018.
v1.2017	11/1/2017	Gwen Fraley, MS, CGC	Quarterly review. No criteria changes. Updated references.
v1.2017	09/15/2017	Megan Czarniecki, MS, CGC	Formatted references to NLM style. Moved methodological considerations to appropriate use criteria and background. Updated associated CPT codes. Approved by Policy Lead.
v1.2017	07/03/2017	Heather Dorsey, MS, CGC	Quarterly review. No criteria changes. Updated references.
v1.2017	04/18/2017	Megan Czarniecki, MS, CGC	Quarterly review. No criteria changes. Updated references.
v1.2017	01/23/2017	Cheryl Thomas, MS, CGC	Quarterly review. No criteria changes. Updated references. Renumbered for 2017.
v1.2016	10/05/2016	Gwen Fraley, MS, CGC	Combined Thrombophilias and Pharmacogenetic testing into same guidelines. Updated references.
v1.2015	10/08/2015	Marie Schuetzle, MS, CGC	Original version

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Primary Author: Marie Schuetzle, MS, CGC