Medica Coverage Policy

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<th>Policy Name:</th>
<th>Pharmacogenetic Testing of the VKORC1 Gene for Warfarin Response</th>
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<td>Effective Date:</td>
<td>4/23/2018</td>
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**Important Information – Please Read Before Using This Policy**

These services may or may not be covered by all Medica plans. Please refer to the member’s plan document for specific coverage information. If there is a difference between this general information and the member’s plan document, the member’s plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless those programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica coverage policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

**Coverage Policy**

Pharmacogenetic testing of the VKORC1 gene for warfarin response is investigative and therefore **NOT COVERED**. There is insufficient reliable evidence in the form of high quality peer-reviewed medical literature to establish the effects on health care outcomes.

**Note:** For CYP2C9 see related Medica coverage policy, *Cytochrome P450 (CYP450) Genotyping*.

**Note:** This policy is no longer scheduled for routine review of the scientific literature.

**Description**

Warfarin is an orally administered anticoagulant drug and is prescribed for the prevention and treatment of thromboembolic events in high-risk individuals. Finding the optimal dose has been confounded by response variability in patients, a narrow therapeutic range, and interaction of warfarin with other drugs and food.

Qualitative, in vitro genetic assays are intended to identify **CYP2C9** and **VKORC1** human gene variants that can alter a patient’s response to warfarin therapy. The theoretical advantage is being able to predict warfarin dosing by helping the physician determine an ideal starting dose reducing the risk of warfarin-related adverse events (e.g. life-threatening bleeds, deep vein thrombosis, and other thromboembolic events). Knowledge of patient’s warfarin response would theoretically decrease the number of office visits and dose adjustments and reduce the time needed to achieve an optimal maintenance dose. A patient’s DNA is isolated from whole blood or saliva using commercially available kits or in-house methods.

**FDA Approval**

Warfarin is an orally administered anticoagulant drug and is prescribed for the prevention and treatment of thromboembolic events in high-risk individuals. Finding the optimal dose has been confounded by response variability in patients, a narrow therapeutic range, and interaction of warfarin with other drugs and food.
Qualitative, in vitro genetic assays are intended to identify CYP2C9 and VKORC1 human gene variants that can alter a patient’s response to warfarin therapy. The theoretical advantage is being able to predict warfarin dosing by helping the physician determine an ideal starting dose reducing the risk of warfarin-related adverse events (e.g. life-threatening bleeds, deep vein thrombosis, and other thromboembolic events). Knowledge of patient’s warfarin response would theoretically decrease the number of office visits and dose adjustments and reduce the time needed to achieve an optimal maintenance dose. A patient’s DNA is isolated from whole blood or saliva using commercially available kits or in-house methods.

FDA Approval
FDA classifies genetic testing systems for warfarin response as “drug metabolizing enzyme genotyping systems” and regulates them as Class II devices. The following warfarin genetic tests and systems that have received FDA 510(k) marketing clearance may include but are not limited to:

Warfarin genetic assay systems:
- INFINITI 2C9 & VKORC1 Multiplex Assay for Warfarin (AutoGenomics, Inc. Vista, CA.)
- Verigene Warfarin Metabolism Nucleic Acid Test and Verigene System (Nanosphere, Inc. Northbrook, IL)
- eSensor 2C9/VKOR Test and eSensor XT-8 System (GenMarkDX Diagnostics, Inc. Carlsbad, CA.)
- TaqMan Drug Metabolism Genotyping Assay (Applied Biosystems Foster City, CA.)
- eQ-PCR LC Warfarin Genotyping Kit (TrimGen Corp. Sparks, MD.)
- Warfarin Genotyping Reagents Single Probe Assay (Idaho Technology, Inc. Salt Lake City UT.)

Warfarin genetic assay kits:
- Rapid Genotyping Assay-CYP2C9 & VKORC1(Paragon DX™, Morrisville, NC)
- Ambry Test/Warfarin Sensitivity (Ambry Genetics (Aliso Viejo, CA.)
- Warfarin GenoSTAT (Iverson Genetics Bothell, WA.)
- Warfarin DoseAdvise Genetic Test (Kimball Genetics, Inc. Denver, CO.)
- PGxPredict: Warfarin (PGx Health Morrisville, NC.)

Independent laboratories offer testing for warfarin response using their own proprietary technology or other companies' platforms:
- ARUP Laboratories (Salt Lake City, UT.) Warfarin Sensitivity (CYP2C9 & VKORC1)/Mutations
- Mayo Medical Laboratories (Rochester, NY): Warfarin Resistance Genotype Reflex Panel
- Quest Diagnostics (Madison N.J.): AccuType Warfarin

Prior Authorization
Prior authorization is not applicable. Claims for this service are subject to retrospective review and denial of coverage, as investigative services are not eligible for reimbursement.

Coding Considerations
Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

CPT Codes:
- 81355 – VKORC1 (vitamin K epoxide reductase complex. Subunit1) (eg, warfarin metabolism), gene analysis, common variants (eg, 1639/3673)

HCPCS Code:
- G9143 - Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)
Pharmacogenetic Testing of the VKORC1 Gene for Warfarin Response

Original Effective Date: 4/1/2009

Re-Review Date(s): 12/20/2011
4/1/2015
3/21/2018
2/20/2020 – administrative update; format

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