Genetic Testing for Initial Warfarin Dose

Prospective review is recommended/required. Please check the member agreement for preauthorization guidelines.

Prospective review is not required.

Description:
Warfarin is administered for preventing and treating thrombo-embolic events in high risk individuals. Warfarin (generic of Coumadin) dosing is a challenging process, due to the narrow therapeutic window, variable response to dosing, and potentially serious bleeding events.

Patients are typically initiated on a starting dose of 2-5 mg and monitored frequently with dose adjustments until a stable International Normalized Ratio (INR) value (a standardized indicator of clotting time) between 2 and 3 is achieved. During this adjustment period, a patient is at high risk for bleeding. Final, stable warfarin dose varies among individuals by more than an order of magnitude. Factors influencing stable dose include body mass index, age, interacting drugs, and indication for therapy. In addition, genetic variants of cytochrome p450 2C9 (CYP2C9) and vitamin K epoxide reductase subunit C1 (VKORC1) genes together account for a substantial proportion of inter-individual variability.

Using the results of CYP2C9 and VKORC1 genetic testing to predict a warfarin starting dose that approximates the individual patient’s likely maintenance dose may benefit patients by decreasing the risk of serious bleeding events and the time to stable INR. Algorithms have also been developed that incorporate not only genetic variation but also other significant factors to predict the best starting dose.

The U.S. Food and Drug Administration (FDA) recently cleared a new genetic test for marketing that will help physicians assess whether a patient may be especially sensitive to warfarin. The Nanosphere Verigene Warfarin Metabolism Nucleic Acid Test detects some variants of both genes. The Nanosphere test is not intended to be a stand-alone tool to determine optimum drug dosage, but should be used along with clinical evaluation and other tools, including INR, to determine the best treatment for patients. The FDA cleared the test based on results of a study conducted by the manufacturer of hundreds of DNA samples as well as on a broad range of published literature. In a three-site study, the test was accurate in all cases where the test yielded a result; 8 percent of the tests could not identify which genetic variants were present.
Medical Criteria:
BlueCHiP For Medicare Members ONLY:

Pharmacoenomic testing of CYP2C9 or VKORC1 alleles to predict warfarin responsiveness is covered for BlueCHiP for Medicare members only who are candidates for anticoagulation therapy with warfarin who are participating in National Institutes of Health (NIH)-sponsored clinical trials, in accordance with the Centers for Medicare and Medicaid Services (CMS) guidelines. Members must meet the clinical trial recruiting criteria established by the National Institutes of Health (NIH). Information regarding trials which are actively recruiting may be found at www.clinicaltrials.gov.

All other members:
Using the results of genetic testing/genotyping (e.g., results from the Nanosphere Verigene Warfarin Metabolism Nucleic Acid Test) for the purpose of guiding the initial warfarin dose, approximating the individual patient’s likely maintenance dose and decreasing the time to stable INR, thus reducing the risk of serious bleeding is considered not medically necessary for all products.

Policy:
BlueCHiP For Medicare Members ONLY:
Pharmacoenomic testing of CYP2C9 or VKORC1 is covered for BlueCHiP for Medicare members only who are participating in National Institutes of Health (NIH)-sponsored clinical trials, in accordance with the Centers for Medicare and Medicaid Services (CMS) guidelines. HCPCS code Q9143 must be filed with the Q0 (Q zero) modifier to indicate the service was performed as part of a clinical trial.

All other members:
Using the results of genetic testing/genotyping (e.g., with The Nanosphere Verigene Warfarin Metabolism Nucleic Acid Test) is considered not medically necessary. The impact of this testing on clinical outcomes and clinical utility is not currently known as there is insufficient published, peer-reviewed scientific literature to demonstrate improved patient outcomes compared to standard treatment without genotyping.

NOTE:
Medicare policy is developed separately from BCBSRI policy. Medicare policy incorporates scientific evidence with local expert opinion, and consideration of governmental regulations from CMS (Centers for Medicare and Medicaid Services), such as national coverage determinations or local coverage determinations. and the US Congress. BCBSRI policy is based upon peer-reviewed, scientifically controlled studies in the literature that demonstrate the superior health outcome of a service or treatment. In addition to benefit differences, CMS may reach different conclusions regarding the scientific evidence than does BCBSRI. BCBSRI and Medicare policies may differ, however, our BlueCHiP for Medicare members must be offered, at least, the same services as Medicare offers. (In some, but not all instances, BCBSRI offer more benefits than does Medicare).
Coverage:
Benefits may vary between groups/contracts. Please refer to the appropriate member certificate/subscriber agreement/Rite Care contract for applicable diagnostic imaging, lab, and machine tests coverage/benefits, and those that address services that are not medically necessary.

Coding:
Covered for BlueCHiP for Medicare members only:

**G9143-Q0** Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)

Not medically necessary for all members:

**G9143** Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)

Related Topics:
International Normalized Ratio (INR)

References:


**Published:**
Policy Update, Nov 2007
Policy Update, Jan 2008
Provider Update, Nov 2009
Provider Update, Jun 2010
Provider Update, Jun 2011

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