MLN Matters®
Information for Medicare Fee-for-Service Health Care Professionals

News Flash – The Centers for Medicare & Medicaid Services (CMS) is listening and wants to hear from you about the services provided by your Medicare Fee-for-Service (FFS) contractor that processes and pays your Medicare claims. CMS is preparing to conduct the fifth annual Medicare Contractor Provider Satisfaction Survey (MCPSS). This survey offers Medicare FFS providers and suppliers an opportunity to give CMS feedback on their interactions with Medicare FFS contractors related to seven key business functions: Provider Inquiries, Provider Outreach & Education, Claims Processing, Appeals, Provider Enrollment, Medical Review, and Provider Audit & Reimbursement. To learn more about the MCPSS, please visit *http://www.cms.hhs.gov/MCPSS* on the CMS website.

MLN Matters® Number: MM6715 Revised | Related Change Request (CR) #: 6715

Related CR Release Date: January 8, 2010 | Effective Date: August 3, 2009

Related CR Transmittal #: R1889CP and R111NCD | Implementation Date: April 5, 2010

Pharmacogenomic Testing for Warfarin Response

Note: This article was revised on January 8, 2010, to reflect a revised CR 6715 that was issued on January 8, 2010. In the article, the CR release date, transmittal numbers (see above), and the Web addresses for accessing the transmittals were changed. All other information remains the same.

Provider Types Affected

Physicians and other providers who bill Medicare contractors (carriers, fiscal intermediaries (FI), or Medicare Administrative Contractors (A/B MAC)) for providing pharmacogenomic testing to predict warfarin (Coumadin®) responsiveness to Medicare beneficiaries should be aware of this article.

What You Need to Know

CR 6715, from which this article is taken, announces that effective August 3, 2009, pharmacogenomic testing to predict warfarin responsiveness is covered only when provided to Medicare beneficiaries in the context of a prospective randomized, controlled clinical study when that study meets certain criteria as outlined in the *Medicare National Coverage Determinations (NCD)* Manual, Chapter 1, Section 90.1 (Pharmacogenomic Testing to Predict Warfarin Responsiveness), which you

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can find as an attachment to CR 6715. Pharmacogenomic testing for warfarin responsiveness is limited to testing for CYP2C9 or VKORC1 alleles. Testing is covered for Medicare beneficiaries who: 1) Are candidates for anticoagulation therapy with warfarin, 2) Have not been previously tested for CYP2C9 or VKORC1 alleles, and 3) Have received fewer than five days of warfarin in the anticoagulation regimen for which the testing is ordered. Pharmacogenomic testing for the presence of the CYP2C9 and VKORC1 alleles to predict warfarin responsiveness is covered only once in a patient's lifetime.

Background

There has been considerable public interest in the use of pharmacogenomic testing (testing of how an individual's genetic makeup, or genotype, affects the body's response to drugs) to predict a patient's response to warfarin sodium (an orally administered anticoagulant drug marketed most commonly as Coumadin®). Warfarin affects the vitamin K-dependent clotting factors II, VII, IX, and X, and is thought to interfere with clotting factor synthesis.

The elimination of warfarin is almost entirely by metabolic conversion to inactive metabolites by cytochrome P450 (CYP) enzymes in liver cells. CYP2C9 is the principal cytochrome P450 enzyme that modulates the anticoagulant activity of warfarin. From results of clinical studies, genetic variation in the *CYP2C9* and/or *VKORC1* genes can, in concert with clinical factors, predict how each individual responds to warfarin.

On August 4, 2008, the Centers for Medicare & Medicaid Services (CMS) opened a National Coverage Analysis (NCA) to determine if the use of pharmacogenomic testing for warfarin responsiveness is reasonable and necessary under the Medicare program. On August 3, 2009, CMS issued a final decision stating that the available evidence does not demonstrate that pharmacogenomic testing to predict warfarin responsiveness improves health outcomes in Medicare beneficiaries, and is therefore <u>not</u> reasonable and necessary under Section1862(a)(1)(A) of the Social Security Act (the Act).

However, the CMS decision also states that the available evidence <u>does</u> support pharmacogenomic testing for warfarin responsiveness under Coverage with Evidence Development (CED). CR 6715 announces that, effective August 3, 2009, the available evidence supports that CED under Section 1862(a)(1)(E) of the Act is appropriate for pharmacogenomic testing of CYP2C9 or VKORC1 alleles to predict warfarin responsiveness by any method, and is therefore covered when provided to Medicare beneficiaries who are candidates for anticoagulation therapy with warfarin only if they have not been previously tested for CYP2C9 or VKORC1 alleles; and have received fewer than five days of warfarin in the anticoagulation regimen for which the testing is ordered.

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Further, such patients must be enrolled in a prospective, randomized, controlled clinical study that addresses one or more aspects of the specific research questions, and the study must adhere to standards of scientific integrity and relevance to the Medicare population. See Publication 100-03, NCD Manual, Chapter 1, section 90.1, for detailed study requirements/criteria.

Note: This NCD does not determine coverage to identify CYP2C9 or VKORC1 alleles for other purposes, nor does it determine national coverage to identify other alleles to predict warfarin responsiveness. Further, CMS believes that the available evidence does not demonstrate that pharmacogenomic testing of CYP2C9 or VKORC1 alleles to predict warfarin responsiveness improves health outcomes in Medicare beneficiaries outside the context of CED, and is therefore not reasonable and necessary under Section 1862(a)(1)(A) of the Act.

Billing Requirements

A new temporary Healthcare Common Procedure Coding System (HCPCS) Level II code effective August 3, 2009, G9143 (warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)), has been developed to enable the implementation of pharmacogenomic testing under CED. Please note that this would be a once-in-a-lifetime test unless there is a reason to believe that the patient's personal genetic characteristics would change over time.

Institutional clinical trial claims for pharmacogenomic testing for warfarin response are identified through the presence of all of the following elements:

- Value Code D4 and 8-digit clinical trial number (when present on the claim);
- ICD-9 diagnosis code V70.7;
- Condition Code 30;
  (For these three elements, please see MM5790 -- Use of an 8-Digit Registry Number on Clinical Trial Claims at *http://www.cms.hhs.gov/MLNMattersArticles/downloads/MM5790.pdf* on the CMS website)
- HCPCS modifier Q0: outpatient claims only (please see MM5805 -- New Healthcare Common Procedure Coding System (HCPCS) Modifiers when Billing for Patient Care in Clinical Research Studies at *http://www.cms.hhs.gov/MLNMattersArticles/downloads/MM5805.pdf* on the CMS website; and
- HCPCS code G9143 (mandatory with the April 2010 Integrated Outpatient Code Editor and the January 2011 clinical laboratory fee schedule (CLFS) updates). Prior to these times, clinical studies should bill Medicare contractors for this test as they currently do absent these instructions, and the Medicare contractors should process and pay those claims accordingly.

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Practitioner clinical trial claims for pharmacogenomic testing for warfarin response are identified through the presence of all of the following elements:

- ICD-9 diagnosis code V70.7;
- 8-digit clinical trial number (when present on the claim);
- HCPCS modifier Q0; and,
- HCPCS code G9143 (to be carrier-priced for claims with dates of service on and after August 3, 2009, processed prior to the January 2011 CLFS update).

Payment Requirements

You should be aware that Medicare will track whether a beneficiary receives once-in-a-lifetime pharmacogenomic testing for warfarin response and will generate a Medicare line-item denial if a subsequent test is submitted for payment. Your carrier, FI, or MAC will provide the following messages to enforce the one-time limitation for the test:

- Claim Adjustment Reason Code (CARC) 50 – These are non-covered services because this is not deemed a 'medical necessity' by the payer. Note: Refer to the 835 Healthcare Policy Identification Segment, if present. (The aforementioned note is a revision to CARC 50 effective 04/01/2010.)
- Remittance Advice Remark Code (RARC) N362 – The number of Days or Units of Service exceeds our acceptable maximum.
- Group Code CO – Contractual Obligation
- Medicare Summary Notice (MSN) 16.76 – This service/item was not covered because you have exceeded the lifetime limit for getting this service/item. (Este servicio/articulo no fue cubierto porque usted ya se ha pasado del limite permitido de por vida para recibirlo.) (MSN 16.76 is effective for dates of service on and after August 3, 2009.)

Additionally, Medicare will return to provider/return as unprocessable claims for pharmacogenomic testing for warfarin response when not billed with HCPCS modifier Q0 (Investigational clinical service provided in a clinical research study that is in an approved clinical research study) on the same line with HCPCS G9143 using the following messages:

- CARC 4 - The procedure code is inconsistent with the modifier used or a required modifier is missing.
- Group Code CO- Contractual Obligation
- MSN 16.77 – This service/item was not covered because it was not provided as part of a qualifying trial/study. (Este servicio/articulo no fue cubierto porque no estaba incluido como parte de un unsayo clinico/estudio calificado.) (MSN 16.77 is effective for dates of service on and after August 3, 2009.)

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If your claim contains the Q0 modifier and HCPCS G9143 but does not contain the V70.7 diagnosis code, those claim lines will generate a return to provider/return as unprocessable with the following messages:

- CARC 16 – Claim/service lacks information which is needed for adjudication. At least one Remark Code must be provided (may be comprised of the NCPDP Reject Reason Code, or Remittance Advice Remark Code that is not an ALERT.) RARC 64 – Missing/incomplete/invalid other diagnosis. Group Code CO – Contractual Obligation, and MSN 16.77 – This service/item was not covered because it was not provided as part of a qualifying trial/study. (Este servicio/articulo no fue cubierto porque no estaba incluido como parte de un unsayo clinico/estudio calificado.) (MSN 16.77 is effective for dates of service on and after August 3, 2009.)

Please note that effective for claims with dates of service August 3, 2009, through April 4, 2010, your contractors will not search their files to adjust previously processed claims, but will adjust any claims that you bring to their attention.

Additional Information

You can find more information about pharmacogenomic testing for warfarin response by going to CR 6715, which was issued in two transmittals. The first transmittal updates the *Medicare National Coverage Determinations Manual*, Chapter 1, Section 90.1 (Pharmacogenomic Testing to Predict Warfarin Responsiveness) and that transmittal is at *http://www.cms.hhs.gov/Transmittals/downloads/R111NCD.pdf* on the CMS website. The second transmittal, *http://www.cms.hhs.gov/Transmittals/downloads/R1889CP.pdf*, updates the *Medicare Claims Processing Manual*, Chapter 32 (Billing Requirements for Special Services), Section 240 (Pharmacogenomic Testing for Warfarin Response).

If you have any questions, please contact your carrier, FI, or MAC at their toll-free number, which may be found at *http://www.cms.hhs.gov/MLNProducts/downloads/CallCenterTollNumDirectory.zip* CMS website.

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