CMS Manual System	Department of Health & Human Services (DHHS)
Pub 100-04 Medicare Claims Processing	Centers for Medicare & Medicaid Services (CMS)
Transmittal 1889	Date: January 8, 2010
	Change Request 6715

Transmittal 1880, dated December 18, 2009, is being rescinded and replaced with Transmittal 1889. The only change is the section numbers on the transmittal under Section II and in the manual text. All other material remains the same.

SUBJECT: PharmacogenomicTesting for Warfarin Response

I. SUMMARY OF CHANGES: There has been considerable public interest in the use of pharmacogenomic testing to predict a patient's response to warfarin, an orally administered anticoagulant drug that is marketed most commonly as Coumadin. Anticoagulant drugs are sometimes referred to as "blood thinners" by the lay public. Pharmacogenomics is the study of how an individual's genetic makeup, or genotype, affects the body's response to drugs. It is an examination of the inherited components and variations in genes that dictate drug/medication response. Pharmacogenomics explores the ways these variations can be used to try to predict whether a patient will have a good response to a drug, a bad response, or no response at all. It is claimed that genetic variability in the CYP2C9 and/or VKORC1genes, in combination with many other factors, may partially predict a patient"s response to warfarin.
On August 4, 2008, CMS opened a National Coverage Analysis.

NEW / REVISED MATERIAL
EFFECTIVE DATE: AUGUST 3, 2009
IMPLEMENTATION DATE: APRIL 5, 2010

Disclaimer for manual changes only: The revision date and transmittal number apply only to red italicized material. Any other material was previously published and remains unchanged. However, if this revision contains a table of contents, you will receive the new/revised information only, and not the entire table of contents.

II. CHANGES IN MANUAL INSTRUCTIONS: (N/A if manual is not updated)
R=REVISED, N=NEW, D=DELETED

R/N/D	CHAPTER / SECTION / SUBSECTION / TITLE
R	32/Table of Contents
N	32/250/Pharmacogenomic Testing for Warfarin Response
N	32/250.1/Coverage Requirements
N	32/250.2/ Billing Requirements
N	32/250.3/Payment Requirements

III. FUNDING:

SECTION A: For Fiscal Intermediaries and Carriers:
No additional funding will be provided by CMS; contractor activities are to be carried out within their operating budgets.

SECTION B: For Medicare Administrative Contractors (MACs):
The Medicare Administrative Contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS does not construe this as a change to the MAC Statement of Work. The contractor is not obligated to incur costs in excess of the amounts allotted in your contract unless and until specifically authorized by the contracting officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the contracting officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

IV. ATTACHMENTS:

Business Requirements
Manual Instruction

Unless otherwise specified, the effective date is the date of service.

Attachment - Business Requirements

Pub. 100-04	Transmittal: 1889	Date: January 8, 2010	Change Request: 6715

Transmittal 1880, dated December 18, 2009, is being rescinded and replaced with Transmittal 1889. The only change is the section numbers on the transmittal under Section II and in the manual text. All other material remains the same.

SUBJECT: PharmacogenomicTesting for Warfarin Response

EFFECTIVE DATE: AUGUST 3, 2009
IMPLEMENTATION DATE: APRIL 5, 2010

I. GENERAL INFORMATION

A. Background: There has been considerable public interest in the use of pharmacogenomic testing to predict a patient's response to warfarin, an orally administered anticoagulant drug that is marketed most commonly as Coumadin. Anticoagulant drugs are sometimes referred to as "blood thinners" by the lay public. Pharmacogenomics is the study of how an individual's genetic makeup, or genotype, affects the body's response to drugs. It is an examination of the inherited components and variations in genes that dictate drug/medication response. Pharmacogenomics explores the ways these variations can be used to try to predict whether a patient will have a good response to a drug, a bad response, or no response at all. It is claimed that genetic variability in the CYP2C9 and/or VKORC1genes, in combination with many other factors, may partially predict a patient's response 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. However, the decision further states that the available evidence does support pharmacogenomic testing for warfarin responsiveness under coverage with evidence development (CED).

B. Policy: Effective August 3, 2009, pharmacogenomic testing to predict warfarin responsiveness is covered only when provided to Medicare beneficiaries who are candidates for anticoagulation therapy with warfarin; 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; and only then in the context of a prospective, randomized, controlled clinical study when that study meets certain criteria as outlined in Pub 100-03, section 90.1, of the NCD Manual.

NOTE: A new temporary HCPCS Level II code effective August 3, 2009, G9143, warfarin responsiveness testing by genetic technique using any method, any number of specimen(s), was developed to enable implementation of CED for this purpose. This is a once-in-a-lifetime test absent any reason to believe that the patient's personal genetic characteristics would change over time.

NOTE: 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) - Refer to Transmittal 310, Change Request 5790, dated January 18, 2008;

- ICD-9 diagnosis code V70.7 - Refer to Transmittal 310, Change Request 5790, dated January 18, 2008;
- Condition Code 30 - Refer to Transmittal 310, Change Request 5790, dated January 18, 2008;
- HCPCS modifier Q0: outpatient claims only - Refer to TR 1418, CR 5805, dated January 18, 2008; and,
- HCPCS code G9143 (mandatory with the April 2010 Integrated Outpatient Code Editor (IOCE) and the January 2011 clinical laboratory fee schedule (CLFS) updates. Prior to these times, any trials should bill FIs for this test as they currently do absent these instructions, and the FIs should process and pay those claims accordingly.)

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 or after August 3, 2009, that are processed prior to the January 2011 CLFS update).

II. BUSINESS REQUIREMENTS TABLE

Use"Shall" to denote a mandatory requirement

Number	Requirement	Responsibility (place an "X" in each applicable column)									
		A/B MAC	DME MAC	FI	CARRIER	RHHI	Shared-System Maintainers				OTHER
							FISS	MCS	VMS	CWF	
6715.1	Effective for claims with dates of service on and after August 3, 2009, contractors shall cover pharmacogenomic testing to predict warfarin responsiveness only in the context of an approved, clinical study, in addition to the coverage criteria outlined in Pub 100-03, section 90.1, of the NCD Manual and chapter 32, section 250, Medicare Claims Processing Manual.	X		X	X						
6715.2	The IOCE and CLFS shall accept HCPCS code G9143, warfarin responsiveness testing by genetic technique using any method, any number of specimen(s), effective for dates of service on or after August 3, 2009.										4/1/2010 IOCE 1/1/2011 CLFS
6715.3	A/B MACs, Carriers and FISS shall create an edit to return to provider/return as unprocessable lines that does not contain a HCPCS modifier Q0 on the same line as HCPCS code G9143.	X		X	X		X	X			
6715.3.1	Based on the edit above, contractors shall use the following messages when line item returning	X		X	X						

Number	Requirement	Responsibility (place an "X" in each applicable column)									
		A/B MAC	DME MAC	FI	CARRIER	RHHI	Shared-System Maintainers				OTHER
							FISS	MCS	VMS	CWF	
	to provider/returning as unprocessable: 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/artículo no fue cubierto porque no estaba incluido como parte de un ensayo clínico/estudio calificado.)										
6715.4	A/B MACs, Carriers and FISS shall create an edit to return to provider/return as unprocessable lines with HCPCS code G9143, modifier Q0, but the claims do not contain ICD-9 CM diagnosis V70.7.	X		X	X		X	X			
6715.4.1	Based on the edit above, contractors shall use the following messages when line item returning to provider/returning as unprocessable: CARC 16 - Claim/service lacks information which is needed for adjudication. At least one Remark Code must be provided (may be comprised of either the NCPDP Reject Reason Code, or Remittance Advice Remark Code that is not an ALERT.) Remark Code 64 - Missing/incomplete/invalid other diagnosis. Group Code CO- Contractual Obligation MSN 16.77 – This service/item was not covered because it was not provided as part of a qualifying	X		X	X						

Number	Requirement	Responsibility (place an "X" in each applicable column)									
		A/B MAC	DME MAC	FI	CARRIER	RHHI	Shared-System Maintainers				OTHER
							FISS	MCS	VMS	CWF	
	trial/study. (Este servicio/artículo no fue cubierto porque no estaba incluido como parte de un ensayo clínico/estudio calificado.)										
6715.5	CWF shall create a new edit to reject a HUOP claim containing a line with HCPCS code G9143 and HCPCS G9143 has already been paid for the same beneficiary.									X	
6715.5.1	A/B MACs, carriers and FISS shall deny line items based on the CWF reject above.	X		X	X		X	X			
6715.5.2	Contractors shall use the following messages when denying lines: <u>Claim Adjustment Reason Code (CARC) 50</u> – 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 April 1, 2010.) <u>Remittance Advice Remark Code (RARC) N362</u> – The number of Days or Units of Service exceeds our acceptable maximum. <u>Group Code CO</u> – Contractual Obligation <u>MSN 16.76</u> – This service/item was not covered because you have exceeded the lifetime limit for getting this service/item. (Este servicio/artículo no fue cubierto porque usted ya se ha pasado del límite permitido de por vida, para recibirlo.)	X		X	X			X			
6715.6	CWF shall create a new edit to reject a HUBC claim containing a line with HCPCS code G9143 and G9143 has already been paid for									X	

Number	Requirement	Responsibility (place an "X" in each applicable column)									
		A/B MAC	DME MAC	FI	CARRIER	RHHI	Shared-System Maintainers				OTHER
							FISS	MCS	VMS	CWF	
	the same beneficiary.										
6715.6.1	Contractors shall deny line items based on the CWF reject above.	X			X			X			
6715.6.2	Contractors shall use the following messages when denying lines: 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 April 1, 2010.) RARC N362 – The number of Days or Units of Service exceeds our acceptable maximum. Group Code CO – Contractual Obligation MSN 16.76 – This service/item was not covered because you have exceeded the lifetime limit for getting this service/item. (Este servicio/artículo no fue cubierto porque usted ya se ha pasado del límite permitido de por vida, para recibirlo.)	X			X			X			
6715.7	CWF shall apply appropriate updates to the "Next Eligibility Dates" file. **NOTE:** Appropriate updates include modifications to the HIMR (PRVN), Provider Inquiry, HUQA, and Extract Records on the Next Generation Desktop (NGD) and the Medicare Beneficiary Database (MBD).						X	X		X	NCH NGD MBD
6715.8	Effective for claims with dates of service August 3, 2009, through April 4, 2010, contractors shall not search their files but shall adjust	X		X	X						

Number	Requirement	Responsibility (place an "X" in each applicable column)									
		A/B MAC	DME MAC	FI	CARRIER	RHHI	Shared-System Maintainers				OTHER
							FISS	MCS	VMS	CWF	
	claims brought to their attention.										

III. PROVIDER EDUCATION TABLE

Number	Requirement	Responsibility (place an "X" in each applicable column)									
		A/B MAC	DME MAC	FI	CARRIER	RHHI	Shared-System Maintainers				OTHER
							FISS	MCS	VMS	CWF	
6715.9	A provider education article related to this instruction will be available at http://www.cms.hhs.gov/MLNMattersArticles/ shortly after the CR is released. You will receive notification of the article release via the established "MLN Matters" listserv. Contractors shall post this article, or a direct link to this article, on their Web site and include information about it in a listserv message within one week of the availability of the provider education article. In addition, the provider education article shall be included in your next regularly scheduled bulletin. Contractors are free to supplement MLN Matters articles with localized information that would benefit their provider community in billing and administering the Medicare program correctly.	X		X	X						

IV. SUPPORTING INFORMATION

Section A: For any recommendations and supporting information associated with listed requirements: ***Use "Should" to denote a recommendation.***

X-Ref Requirement Number	Recommendations or other supporting information:
6715.3.1 6715.4.1	MSN 16.77 is effective for dates of service on and after August 3, 2009.
6715.5.2 6715.6.2	MSN 16.76 is effective for dates of service on and after August 3, 2009.

Section B: For all other recommendations and supporting information: N/A

V. CONTACTS

Pre-Implementation Contact(s): Maria Ciccanti, Coverage, 410-786-3107, maria.ciccanti@cms.hhs.gov , Patricia Brocato-Simons, Coverage, 410-786- 0261, patricia.brocatosimons@cms.hhs.gov., Michelle Atkinson, Coverage, 410-786-2881, michelle.atkinson@cms.hhs.gov, Bridgitte Davis, Practitioner Claims, 410-786-4573, bridgitte.davis@cms.hhs.gov, Diana Motsiopoulos, insitutional Claims, 410-786-3379, diana.motsiopoulos@cms.hhs.gov, Joe Bryson, institutional Claims, 410-786-2986, joseph.bryson@cms.hhs.gov, Felicia Rowe, Supplier Claims, 410-786-5655, felicia.rowe@cms.hhs.gov.

Post-Implementation Contact(s): Regional offices

VI. FUNDING

Section A: For *Fiscal Intermediaries (FIs), Regional Home Health Intermediaries (RHHIs),* and/or *Carriers*:

No additional funding will be provided by CMS; contractor activities are to be carried out within their operating budgets.

Section B: *For Medicare Administrative Contractors (MACs)*:

The Medicare Administrative Contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS does not construe this as a change to the MAC Statement of Work. The contractor is not obligated to incur costs in excess of the amounts allotted in your contract unless and until specifically authorized by the contracting officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the contracting officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

Medicare Claims Processing Manual

Chapter 32 – Billing Requirements for Special Services

Table of Contents
(Rev. 1889, 01-08-10)

250 – Pharmacogenomic Testing for Warfarin Response

(Rev. 1889, Issued: 01-08-10; Effective Date: 08-03-09; Implementation Date: 04-05-10)

250.1 – Coverage Requirements

(Rev. 1889, Issued: 01-08-10; Effective Date: 08-03-09; Implementation Date: 04-05-10)

Effective August 3, 2009, pharmacogenomic testing to predict warfarin responsiveness is covered only when provided to Medicare beneficiaries who are candidates for anticoagulation therapy with warfarin; i.e., 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; and only then in the context of a prospective, randomized, controlled clinical study when that study meets certain criteria as outlined in Pub 100-03, section 90.1, of the NCD Manual.

NOTE: *A new temporary HCPCS Level II code effective August 3, 2009, G9143, warfarin responsiveness testing by genetic technique using any method, any number of specimen(s), was developed to enable implementation of CED for this purpose.*

250.2 – Billing Requirements

(Rev. 1889, Issued: 01-08-10; Effective Date: 08-03-09; Implementation Date: 04-05-10)

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) - Refer to Transmittal 310, Change Request 5790, dated January 18, 2008;*

- *ICD-9 diagnosis code V70.7 - Refer to Transmittal 310, Change Request 5790, dated January 18, 2008;*

- *Condition Code 30 - Refer to Transmittal 310, Change Request 5790, dated January 18, 2008;*

- *HCPCS modifier Q0: outpatient claims only - Refer to Transmittal 1418, Change Request 5805, dated January 18, 2008; and,*

- *HCPCS code G9143 (mandatory with the April 2010 Integrated Outpatient Code Editor (IOCE) and the January 2011 Clinical Laboratory Fee Schedule (CLFS) updates. Prior to these times, any trials should bill FIs for this test as they currently do absent these instructions, and the FIs should process and pay those claims accordingly.)*

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, that are processed prior to the January 2011 CLFS update.)*

250.3 – Payment Requirements

(Rev. 1889, Issued: 01-08-10; Effective Date: 08-03-09; Implementation Date: 04-05-10)

Beginning April 5, 2010, for claims with dates of service on and after August 3, 2009, the Medicare Shared System will track the number of times a beneficiary receives pharmacogenomic testing for warfarin response. When a claim is received for pharmacogenomic testing for warfarin response, and the shared system has determined that the beneficiary has already received the test in his/her lifetime, it will generate a Medicare line-item denial and the Medicare contractor 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. This change to be effective April 1, 2010: 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.*

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/artículo no fue cubierto porque usted ya se ha pasado del límite permitido de por vida, para recibirlo.).

The Medicare shared system and the carriers will also ensure that pharmacogenomic testing for warfarin response is billed in accordance with clinical trial reporting requirements. In other words, the shared system and the carriers will return to provider/return as unprocessable lines for pharmacogenomic testing for warfarin response when said line is not billed with HCPCS modifier Q0 and ICD-9 CM diagnosis code V70.7 is not present as a secondary diagnosis. When the system or the carrier initiates the line-item return to provider or returns the claim as unprocessable, the Medicare contractor will respond with the following messages:

For a missing QO modifier:
CARC 4 - The procedure code is inconsistent with the modifier used or a required modifier is missing.

For a missing V70.7 diagnosis code when a HCPCS Q0 modifier is reported with HCPCS G9143:

CARC 16 - Claim/service lacks information which is needed for adjudication. At least one Remark Code must be provided (may be comprised of either the NCPDP Reject Reason Code, or Remittance Advice Remark Code that is not an ALERT.)

Remark Code 64 - Missing/incomplete/invalid other diagnosis.

For either a missing Q0 modifier and/or a missing V70.7 diagnosis code:

- *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/artículo no fue cubierto porque no estaba incluido como parte de un ensayo clínico/estudio calificado.)*