CMS Manual System	Department of Health & Human Services (DHHS)
Pub 100-02 Medicare Benefit Policy	Centers for Medicare & Medicaid Services (CMS)
Transmittal 120	**Date: January 29, 2010**
	Change Request 6806

SUBJECT: Revision of Definition of Compendia as Authoritative Source for Use in the Determination of a Medically-Accepted Indication of Drugs/Biologicals Used Off-label in Anti-Cancer Chemotherapeutic Regimens

I. SUMMARY OF CHANGES: Effective January 1, 2010, pursuant to section 182(b) of MIPPA, CMS is making corresponding revisions in Pub. 100-02, Medicare Benefit Policy Manual, chapter 15, section 50.4.5, for use in the determination of a medically-accepted indication of drugs and biologicals used off-label in an anti-cancer chemotherapeutic regimen.

New / Revised Material
Effective Date: January 1, 2010
Implementation Date: March 1, 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	15/50.4.5.1/Process for Amending the List of Compendia for Determination of Medically-Accepted Indications for Off-Label Uses of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen

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. 100-02	Transmittal: 120	Date: January 29, 2010	Change Request: 6806

SUBJECT: Revision of Definition of Compendia as Authoritative Source for Use in the Determination of a Medically-Accepted Indication of Drugs/Biologicals Used Off-label in Anti-Cancer Chemotherapeutic Regimens

Effective Date: January 1, 2010

Implementation Date: March 1, 2010

I. GENERAL INFORMATION

A. Background: Section 1861(t)(2)(B)(ii)(I) of the Social Security Act (the Act), as amended by section 6001(f)(1) of the Deficit Reduction Act of 2005, Pub. Law 109-171, recognizes three compendia-- American Medical Association Drug Evaluations (AMA-DE), United States Pharmacopoeia-Drug Information (USP-DI) or its successor publication, and American Hospital Formulary Service-Drug Information (AHFS-DI)—plus other authoritative compendia as identified by the Secretary, as authoritative sources for use in the determination of a "medically-accepted indication" of drugs and biologicals used off-label in an anti-cancer chemotherapeutic regimen, unless the Secretary has determined that the use is not medically appropriate or the use is identified as not indicated in one or more such compendia.

In the Physician Fee Schedule final rule for calendar year 2008, CMS established a process for revising the list of compendia, as authorized under section 1861(t)(2) of the Act, and also established a definition for "compendium." Under 42 CFR 414.930(a), a compendium is defined "as a comprehensive listing of FDA-approved drugs and biologicals or a comprehensive listing of a specific subset of drugs and biologicals in a specialty compendium, for example, a compendium of anti-cancer treatment." A compendium: (1) includes a summary of the pharmacologic characteristics of each drug or biological and may include information on dosage, as well as recommended or endorsed uses in specific diseases; and, (2) is indexed by drug or biological. In addition, CMS increased the transparency of the process by incorporating a list of desirable compendium characteristics outlined by the Medicare Evidence Development and Coverage Advisory Committee (MedCAC) on March 30, 2006, as criteria for decision-making.

Although the MedCAC desirable characteristics for compendia included reference to conflict of interest and transparency, section 182(b) of the Medicare Improvements for Patients and Providers Act (MIPPA) amended Section 1861(t)(2)(B) of the Act by adding at the end the following new sentence: 'On and after January 1, 2010, no compendia may be included on the list of compendia under this subparagraph unless the compendia has a publicly transparent process for evaluating therapies and for identifying potential conflicts of interests.' For additional background information, consult CR 6191, Transmittal 96, issued October 24, 2008.

B. Policy: Effective January 1, 2010, pursuant to section 182(b) of MIPPA, CMS is making corresponding revisions in Pub. 100-02, Medicare Benefit Policy Manual, chapter 15, section 50.4.5.1, for use in the determination of medically-accepted indications of drugs and biologicals used off-label in anti-cancer chemotherapeutic regimens. See 74 FR 61901.

II. BUSINESS REQUIREMENTS 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	
6806.1	Effective January 1, 2010, contractors shall be aware that the definition of "compendia" has been revised to include a publicly transparent process for evaluating therapies and for identifying potential conflicts of interest. No compendia may be included on the list of compendia without the above criteria being met.	X	X	X	X	X					

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	
6806.2	Contractors shall post this entire instruction, or a direct link to this instruction, on their Web site and include information about it in a listserv message within 1 week of the release of this instruction. In addition, the entire instruction must be included in your next regularly scheduled bulletin. Contractors are free to supplement it with localized information that would benefit their provider community in billing and administering the Medicare program correctly.	X	X	X	X	X					

IV. SUPPORTING INFORMATION

Section A: For any recommendations and supporting information associated with listed requirements, use the box below:
Use "Should" to denote a recommendation.

X-Ref Requirement Number	Recommendations or other supporting information:

Section B: For all other recommendations and supporting information, use this space:

V. CONTACTS

Pre-Implementation Contact(s): Brijet Burton, coverage, 410-786-7364, brijet.burton2@cms.hhs.gov, Pat Brocato-Simons, coverage, 410-786-0261, patricia.brocatosimons@cms.hhs.gov

Post-Implementation Contact(s): CMS ROs

VI. FUNDING

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

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.

50.4.5.1 - Process for Amending the List of Compendia for Determination of Medically-Accepted Indications for Off-Label Uses of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen

(Rev.120, Issued: 01-29-10, Effective:01-01-10, Implementation: 03-01-10)

A. Background

In the Physician Fee Schedule final rule for calendar year *(CY)* 2008, the CMS established a process for revising the list of compendia, as authorized under section 1861(t)(2) of the Social Security Act, and also established a definition for "compendium." At 42 CFR 414.930(a), a compendium is defined "as a comprehensive listing of FDA-approved drugs and biologicals or a comprehensive listing of a specific subset of drugs and biologicals in a specialty compendium, for example, a compendium of anti-cancer treatment." A compendium: (1) includes a summary of the pharmacologic characteristics of each drug or biological and may include information on dosage, as well as recommended or endorsed uses in specific diseases; (2) is indexed by drug or biological, and, *(3) effective January 1, 2010, pursuant to section 182(b) of the Medicare Improvements for Patients and Providers Act (MIPPA), has a publicly transparent process for evaluating therapies and for identifying potential conflicts of interests*. See 42 CFR 414.930(a); 72 FR 66222, 66404, *and 74 FR 61901*.

B. Desirable Characteristics of Compendia

CMS increased the transparency of the process by incorporating a list of desirable compendium characteristics outlined by the Medicare Evidence Development and Coverage Advisory Committee (MedCAC) as criteria for decision-making. The list of desirable compendium characteristics was developed by the MedCAC during a public session on March 30, 2006. T he goal of this session was to review the evidence and advise CMS on the desirable characteristics of compendia for use in the determination of medically accepted indications of drugs and biologicals in anti-cancer therapy. As a result of this meeting, the MedCAC generated the following list of desirable characteristics:

- Extensive breadth of listings,
- Quick processing from application for inclusion to listing,
- Detailed description of the evidence reviewed for every individual listing,
- Use of pre-specified published criteria for weighing evidence,
- Use of prescribed published process for making recommendations,
- Publicly transparent process for evaluating therapies,
- Explicit "Not Recommended" listing when validated evidence is appropriate,
- Explicit listing and recommendations regarding therapies, including sequential use or combination in relation to other therapies,
- Explicit "Equivocal" listing when validated evidence is equivocal, and,

- Process for public identification and notification of potential conflicts of interest of the compendias' parent and sibling organizations, reviewers, and committee members, with an established procedure to manage recognized conflicts.

Furthermore, the provisions discussed in section 182(b) of MIPPA bring more uniformity in compendia conflict of interest disclosure practices and allow the public the ability to monitor how these policies impact compendia off-label recommendations.

C. Process for Changing List of Compendia

CMS will provide an annual 30-day open request period starting January 15 for the public to submit requests for additions or deletions to the compendia list contained on the CMS Web site at http://www.cms.hhs.gov/CoverageGenInfo/02_compendia.asp.

Complete requests as defined in section 50.4.5.1.D will be posted to the Web site *annually* by March 15 for public notice and comment. The request will identify the requestor and the requested action *CMS is being asked to make* to the list. Public comments will be accepted for a 30-day period beginning on the day the request is posted on the Web site. In addition to the annual process, CMS may generate a request for changes to the list at any time an urgent action is needed to protect the interests of the Medicare program and its beneficiaries.

D. Content of Requests

For a request to be considered complete, and therefore accepted for review, it must include the following information:

- The full name and contact information (including the mailing address, e-mail address, and telephone number) of the requestor. If the requestor is not an individual person, the information shall identify the officer or other representative who is authorized to act for the requestor on all matters related to the request.

- Full identification of the compendium that is the subject of the request, including name, publisher, edition if applicable, date of publication, and any other information needed for the accurate and precise identification of the specific compendium.

- A complete, written copy of the compendium that is the subject of the request. If the complete compendium is available electronically, it may be submitted electronically in place of hard copy. If the compendium is available online, the requestor may provide CMS with electronic access by furnishing at no cost to the Federal Government sufficient accounts for the purposes and duration of the review of the application in place of hard copy.

- The specific action that the requestor wishes CMS to take, for example to add or delete a specific compendium.

- Detailed, specific documentation that the compendium that is the subject of the request does or does not comply with the conditions of this rule. Broad, nonspecific claims without supporting documentation cannot be efficiently reviewed; therefore, they will not be accepted.

- *A publicly transparent process for evaluating therapies, which includes the following: (1) internal or external request for listing of a therapy recommendation, including criteria used to evaluate the request (the complete application), (2) listing of all the evidentiary materials reviewed or considered for inclusion in the compendium (3) listing of all individuals who substantively participated in the review and development of the request, and (4) minutes and voting records of meetings for the review and disposition of the request. The information from an internal or external request for inclusion of a therapy in a compendium are available to the public for a period of not less than 5 years, which includes availability on the compendium's Web site for a period of not less than 3 years, coincident with the compendium's publication.*

- *A publicly transparent process for identifying potential conflicts of interests that provides: (1) direct or indirect financial relationships, and (2) ownership or investment interests that exist between individuals or the spouse or minor child of individuals who have substantively participated in the development or disposition of compendia recommendations, and the manufacturer or seller of the drug or biological being reviewed by the compendium. This information shall be identified and made timely available in response to a public request for a period of not less than 5 years, which includes availability on the compendium's Web site for a period of not less than 3 years, coincident with the compendium's publication.*

A request may have only a single compendium as its subject. This will provide greater clarity to the scope of the Agency's review of a given request. A requestor may submit multiple requests, each requesting a different action.

E. Submission of Requests

Requests must be in writing and submitted in one of the following two ways (no duplicates please):

1. Electronic requests are encouraged to facilitate administrative efficiency. Each solicitation will include the electronic address for submissions.

2. *Hard copy requests can be sent to: Centers for Medicare & Medicaid Services, Coverage and Analysis Group, Mailstop C1–09–06, 7500 Security Boulevard, Baltimore, MD 21244.*

Allow sufficient time for hard copies to be received prior to the close of the open request period.

F. Review of Requests

CMS will consider a compendium's attainment of the desirable characteristics specified in 50.4.5.1.B when reviewing requests. CMS may consider additional, reasonable factors in making a determination. For example, CMS may consider factors that are likely to impact the compendium's suitability for this use, such as a change in *the compendium's* ownership or affiliation, *and* the standards applicable to the evidence considered by the compendium. CMS may consider that broad accessibility by the general public to the information contained in the compendium may assist beneficiaries, their treating physicians, or both, in choosing among treatment options. CMS will also consider a compendium's grading of evidence used in making recommendations regarding off-label uses, and the process by which the compendium grades the evidence. CMS may, at its discretion, combine and consider multiple requests that refer to the same compendium, even if those requests are for different actions. This facilitates administrative efficiency in the review of requests.

G. Publishing Review Results

CMS will publish decisions on the CMS Web site within 90 days after the close of the public comment period.

(This instruction was last reviewed by CMS in *December* 2009.)