Medicare Learning Network
MLN Matters
CMS
Information for Medicare Fee-for-Service Health Care Professionals

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Related CR Release Date: October 24, 2008 **Effective Date: June 5, June 10, and July 2, 2008 (see below)**

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Compendia 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

Note: This article was revised on February 15, 2018, to update Web addresses. All other information remains the same.

Provider Types Affected

Physicians, providers, and suppliers submitting claims to Medicare contractors (carriers, DME Medicare Administrative Contractors (DME MACs), Fiscal Intermediaries (FIs), and/or Part A/B Medicare Administrative Contractors (A/B MACs)) for services provided to Medicare beneficiaries.

Provider Action Needed

STOP – Impact to You

This article is based on Change Request (CR) 6191 which updates the list of compendia recognized as authoritative sources of information for the determination of drugs and biologicals used off-label in anti-cancer chemotherapeutic regimens.

CAUTION – What You Need to Know

The Centers for Medicare & Medicaid Services (CMS) is recognizing the following as authoritative compendia and listing them in the 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:

- American Hospital Formulary Service-Drug Information (AHFS-DI), (existing)

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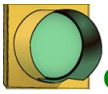
- National Comprehensive Cancer Network **(**NCCN) Drugs and Biologics Compendium, (effective June 5, 2008)
- Thomson Micromedex DrugDex, (effective June 10, 2008) and
- Clinical Pharmacology (effective July 2, 2008).



GO – What You Need to Do

See the Background and Additional Information Sections of this article for further details regarding these changes.

Background

In the past, the following three compendia were recognized 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 of the Department of Health and Human Services determined that the use was not medically appropriate or the use was identified as not indicated in one or more such compendia):

1. American Medical Association Drug Evaluations (AMA-DE),
2. United States Pharmacopoeia-Drug Information (USP-DI) or its successor publication, and
3. American Hospital Formulary Service-Drug Information (AHFS-DI).

Because the AMA-DE and the USP-DI are no longer published (due to changes in the pharmaceutical reference industry), the AHFS-DI became the only remaining statutorily-named compendia available for the CMS to use as a reference. Consequently, CMS received requests from the stakeholder community for a process to revise the list of recognized authoritative compendia.

In the Medicare Physician Fee Schedule final rule for calendar year 2008, CMS established:

- A process for revising the list of compendia. (Section 1861(t)(2) of the Social Security Act; [***http://www.ssa.gov/OP_Home/ssact/title18/1861.htm***], and
- A definition for "compendium." (72 FR 66222 [***http://edocket.access.gpo.gov/2007/07-5506.htm***], 72 FR 66303-66306 [**http://www.cms.gov/Medicare/Coverage/CoverageGenInfo/Downloads/compendiapreamble.pdf*],*** and 72 FR 66404 [**http://www.cms.gov/Medicare/Coverage/CoverageGenInfo/Downloads/compendiareg.pdf*].***

  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

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a specialty compendium, for example, a compendium of anti-cancer treatment." (42 CFR 414.930(a) [***http://edocket.access.gpo.gov/2007/pdf/07-3274.pdf***].

In addition, 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. (42 CFR 414.930(a) [***http://edocket.access.gpo.gov/2007/pdf/07-3274.pdf***], 72 FR 66222 [***http://edocket.access.gpo.gov/2007/07-5506.htm***], and 72 FR 66404 [**http://www.cms.gov/Medicare/Coverage/CoverageGenInfo/Downloads/compendiareg.pdf**].

During a public meeting on March 30, 2006, the Medicare Evidence Development and Coverage Advisory Committee (MedCAC) generated a list of desirable characteristics to use when reviewing a compendium. Subsequently, the MedCAC advised CMS of their findings and recommendations regarding the desirable characteristics of compendia for use in the determination of medically-accepted indications of drugs and biologicals in anti-cancer therapy.

After CMS conducted a review of specific compendia and compared their characteristics with the MedCAC list of desirable characteristics, CMS determined the following are recognized as authoritative compendia and is listing them in the 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:

- American Hospital Formulary Service - Drug Information (AHFS-DI),
- National Comprehensive Cancer Network **(**NCCN) Drugs and Biologics Compendium,
- Thomson Micromedex DrugDex, and
- Clinical Pharmacology.

The above listed compendia employ various rating and recommendation systems that may not be readily cross-walked from compendium to compendium. In general, a use is identified by a compendium as **medically accepted** if the:

- Indication is a Category 1 or 2A in NCCN, or Class I, Class IIa, or Class IIb in DrugDex; or,
- Narrative text in AHFS-DI or Clinical Pharmacology is supportive.

A use is **not medically accepted** by a compendium if the:

- Indication is a Category 3 in NCCN or a Class III in DrugDex; or,

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- Narrative text in AHFS or Clinical Pharmacology is "not supportive."

The complete absence of narrative text on a use is considered neither supportive nor non-supportive.

Medicare contractors may also identify off-label uses that are supported by clinical research under the conditions identified in Section 50.4.5 of the Medicare Benefits Policy Manual, as amended by CR6191. Peer-reviewed medical literature may appear in scientific, medical, and pharmaceutical publications in which original manuscripts are published, only after having been critically reviewed for scientific accuracy, validity, and reliability by unbiased, independent experts prior to publication.

In-house publications of entities whose business relates to the manufacture, sale, or distribution of pharmaceutical products are excluded from consideration. Abstracts (including meeting abstracts) are excluded from consideration.

In determining whether an off-label use is supported, Medicare contractors will evaluate the evidence in published, peer-reviewed medical literature listed in the revised Section 50.4.5.C, which is attached to CR6191. When evaluating this literature, Medicare contractors will consider (among other things) the following:

- Whether the clinical characteristics of the beneficiary and the cancer are adequately represented in the published evidence.
- Whether the administered chemotherapy regimen is adequately represented in the published evidence.
- Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients.
- Whether the study is appropriate to address the clinical question.

Additional Information

The official instruction, CR 6191, issued to your carrier, FI, A/B MAC, and DME MAC regarding this change may be viewed at **http://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/downloads/R96BP.pdf** on the CMS website. The revised sections of the Medicare Benefit Policy Manual are attached to CR 6191.

If you have any questions, please contact your carrier, FI, A/B MAC, or DME MAC at their toll-free number, which may be found at **http://www.cms.gov/Research-Statistics-Data-and-Systems/Monitoring-Programs/provider-compliance-interactive-map/index.html** on the CMS website.

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Document History

- November 12, 2008 – Initial article released.
- February 15, 2018 – The article is revised to update Web addresses. All other information remains the same.

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