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 – JA6191

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Effective Dates:
June 5, 2008 - NCCN Drugs and Biologics Compendium
June 10, 2008 - Thomson Micromedex DrugDex
July 2, 2008 - Clinical Pharmacology

Implementation Date: November 25, 2008

Key Words	MM6191, CR6191, R96BP, Compendia, Drugs, Biologicals, Off-label, Anti-cancer, Chemotherapeutic, Cancer
Contractors Affected	• Fiscal Intermediaries (FIs) • Medicare Carriers • Durable Medical Equipment Medicare Administrative Contractors (DME MACs) • Part A/B MACs
Provider Types Affected	Physicians, providers, and suppliers submitting claims to Medicare Carriers, DME MACs, FIs, and/or A/B MACs for services provided to Medicare beneficiaries

Change Request (CR) 6191 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.

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);
- 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**).

Provider Needs to Know…

- 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.hhs.gov/CoverageGenInfo/Downloads/compendiapreamble.pdf*); and (72 FR 66404: *http://www.cms.hhs.gov/CoverageGenInfo/Downloads/compendiareg.pdf*)).
- A compendium is defined "as a comprehensive listing of the Food and Drug Administration-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" (42 Code of Federal Regulations (CFR) 414.930(a): *http://edocket.access.gpo.gov/2007/pdf/07-3274.pdf*).
- In addition, a compendium:
  - 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
  - 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.hhs.gov/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:
  - AHFS-DI,
  - 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
  - Narrative text in AHFS or Clinical Pharmacology is "not supportive."

Note: 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; and
  - Whether the study is appropriate to address the clinical question.

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):
	  • American Medical Association Drug Evaluations (AMA-DE),
	  • United States Pharmacopoeia-Drug Information (USP-DI) or its successor

	publication, and • 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 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.
Operational Impact	N/A
Reference Materials	The related MLN Matters article can be found at *http://www.cms.hhs.gov/MLNMattersArticles/downloads/MM6191.pdf* on the CMS website. The official instruction (CR6191) issued regarding this change may be found at *http://www.cms.hhs.gov/Transmittals/downloads/R96BP.pdf* on the CMS website. The *Medicare Benefit Policy Manual,* Chapter 15 *(*Covered Medical and Other Health Services), §50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen), and §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) is attached to CR6191.