

Coverage of Drugs and Biologicals for Label and Off-Label Uses

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Policy Summary

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Overview

Drugs and biologicals must be determined to meet the statutory definition. Under the statute §1861(t) (1), payment may be made for a drug or biological only where it is included, or approved for inclusion, in the latest official edition of the United States Pharmacopoeia National Formulary (USP-NF), the United States Pharmacopoeia-Drug Information (USD-DI), or the American Dental Association (AOA) Guide to Dental Therapeutics, except for those drugs and biologicals unfavorably evaluated in the ADA Guide to Dental Therapeutics. The inclusion of an item in the USP DI does not necessarily mean that the item is a drug or biological. The USP DI is a database of drug information developed by the U.S. Pharmacopoeia but maintained by Micromedex, which contains medically accepted uses for generic and brand name drug products. Inclusion in such reference (or approval by a hospital committee) is a necessary condition for a product to be considered a drug or biological under the Medicare program, however, it is not enough. Rather, the product must also meet all other program requirements to be determined to be a drug or biological. Combination drugs are also included in the definition of drugs if the combination itself or all of the therapeutic ingredients of the combination are included, or approved for inclusion, in any of the above drug compendia.

Drugs and biologicals are considered approved for inclusion in a compendium if approved under the established procedure by the professional organization responsible for revision of the compendium.

An off-label/unlabeled use of a drug is defined as a use for a non-FDA approved indication, that is, one that is not listed on the drug's official label/prescribing information. An indication is defined as a diagnosis, illness, injury, syndrome, condition, or other clinical parameter for which a drug may be given. Off-label use is further defined as giving the drug in a way that deviates significantly from the labeled prescribing information for a particular indication. This includes but is not necessarily limited to, dosage, route of administration, duration and frequency of administration, and population to whom the drug would be administered. Drugs used for indications other than those in the approved labeling may be covered under Medicare if it is

determined that the use is medically accepted, taking into consideration the major drug compendia, authoritative medical literatures and/or accepted standards of medical practice. Determinations as to whether medication is reasonable and necessary for an individual patient are made on appeal on the same basis as all other such determinations (i.e., with support from the peer-reviewed literature, with the advice of medical consultants, with reference to accepted standards of medical practice, and in consideration of the medical circumstance of the individual case).

Guidelines

Use of the drug or biological must be safe and effective and otherwise reasonable and necessary. (See the Medicare Benefit Policy Manual, Chapter 16, "General Exclusions from Coverage," §20.) Drugs or biologicals approved for marketing by the Food and Drug Administration (FDA) are considered safe and effective for purposes of this requirement when used for indications specified on the labeling. Therefore, the program may pay for the use of an FDA approved drug or biological, if:

- It was injected on or after the date of the FDA's approval;
- It is reasonable and necessary for the individual patient; and
- All other applicable coverage requirements are met.

An unlabeled use of a drug is a use that is not included as an indication on the drug's label as approved by the FDA. FDA approved drugs used for indications other than what is indicated on the official label may be covered if the contractor determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice. The following guidelines identify three categories in which medications would not be reasonable and necessary according to accepted standards of medical practice.

- Not for Particular Illness – Medications given for a purpose other than the treatment of a particular condition, illness, or injury are not covered (except for certain immunizations).
- Injection Method Not Indicated – Medication given by injection (parenterally) is not covered if standard medical practice indicates that the administration of the medication by mouth (orally) is effective and is an accepted or preferred method of administration.
- Excessive Medications – Medications administered for treatment of a disease which exceed the frequency or duration of injections indicated by accepted standards of medical practice are not covered.

If a medication is determined not to be reasonable and necessary for diagnosis or treatment of an illness or injury according to these guidelines, the entire charge will be excluded (i.e., for both the drug and its administration). Also excluded from payment is any charge for other services (such as office visits) which are primarily for the purpose of administering a non-covered injection (i.e., an injection that is not reasonable and necessary for the diagnosis or treatment of an illness or injury).

Effective January 1, 1994, off-label, medically accepted indications of Food and Drug Administration-(FDA) approved drugs and biologicals used in an anti-cancer chemotherapeutic regimen are identified under the indications described below. A regimen is a combination of anti-cancer agents clinically recognized for the treatment of a specific type of cancer. Off-label, medically accepted indications are supported in either one or more of the compendia or in peer-reviewed medical literature. The contractor may maintain its own subscriptions to the listed compendia or peer-reviewed publications to determine the medically accepted indication of drugs or biologicals used off-label in an anti-cancer chemotherapeutic regimen. Compendia documentation or peer-reviewed literature supporting off-label use by the treating physician may also be requested of the physician by the contractor.

Coverage Indications

A medically accepted indication is one of the following:

- An FDA approved, labeled indication or a use supported in the American Hospital Formulary Service Drug Information (AHFS-DI), NCCN Drugs and Biologics Compendium, Truven Health Analytics Micromedex Drug Dex®, Elsevier/Gold Standard Clinical Pharmacology and Wolters Kluwer Lexi-Drugs® as the acceptable compendia based on CMS' Change Request 6191 (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); or
- Articles or Local Coverage Determinations (LCDs) published by CMS.

The compendia listed above will be accepted at the following levels:

- American Hospital Formulary Service-Drug Information (AHFS-DI) – indication is supportive
- NCCN Drugs and Biologics Compendium - indication is a Category 1 or 2A

- Micromedex DrugDex® – indication is Class I, Class IIa, or Class IIb
- Clinical Pharmacology – indication is supportive
- Lexi-Drugs - indication is rated as “Evidence Level A”

When new off-label uses for drugs are published in the above compendia at the accepted level of recommendation, the effective date of those off-label uses is the date of publication of our revised coverage, not the date of inclusion in the compendia.

Coverage Limitations

If a use is identified as not indicated by CMS or the FDA, or if a use is specifically identified as not indicated in one or more of the compendia listed, or if the contractor determines, based on peer-reviewed medical literature, that a particular use of a drug is not safe and effective, the off-label use is not supported and the drug will not be covered.

Regardless of the evidence supporting coverage for a particular off-label use, payment may only be made if the use is reasonable and necessary for the treatment of illness or injury of the specific patient receiving the drug.

Services related to non-covered services or drugs are also not covered (e.g., administration services).

References

CMS Local Coverage Determinations (LCDs) and Articles

LCD	Article	Contractor	Medicare Part A	Medicare Part B
L33915 Label and Off-label Coverage of Outpatient Drugs and Biologicals	A56744 Billing and Coding: Label and Off-label Coverage of Outpatient Drugs and Biologicals	First Coast	FL, PR, VI	FL, PR, VI
L33394 Drugs and Biologicals, Coverage of, for Label and Off-Label Uses	A52855 Billing and Coding: Drugs and Biologicals	NGS	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI
N/A	A53049 Approved Drugs and Biologicals; Includes Cancer Chemotherapeutic Agents	Novitas	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX
N/A	A52425 (Drugs and Biologicals, Coverage of, for Label and Off-Label Uses - Supplemental Instructions Article) Retired 06/07/2020	CGS	KY, OH	KY, OH
	A52532 (Off-Label Cancer Chemotherapy Use) Retired 06/07/2020			

CMS Benefit Policy Manual

[Chapter 9: § 40.1.6 Medical Appliances and Supplies](#)

[Chapter 15: § 50 Drugs and Biologicals](#)

[Chapter 16: § 20 Services Not Reasonable and Necessary](#)

CMS Claims Processing Manual

[Chapter 17 Drugs and Biologicals](#)

UnitedHealthcare Commercial Policy

[Off-Label/Unproven Specialty Drug Treatment](#)

Related Medicare Advantage Policy Guidelines

[Aprepitant for Chemotherapy-Induced Emesis \(NCD 110.18\)](#)

[Autologous Cellular Immunotherapy Treatment \(NCD 110.22\)](#)

[Avastin® \(Bevacizumab\)](#)

[Camptosar® \(Irinotecan\)](#)

[Dimethyl Sulfoxide \(DMSO\) \(NCD 230.12\)](#)

[Eloxatin® \(Oxaliplatin\)](#)

[Erbix® \(Cetuximab\)](#)

[Erythropoietin Stimulating Agent \(ESA\)](#)

[Erythropoiesis Stimulating Agents \(ESAs\) in Cancer and Related Neoplastic Conditions \(NCD 110.21\)](#)

[Eylea® \(Aflibercept\)](#)

[Halaven® \(Eribulin Mesylate\)](#)

[Intravenous Immune Globulin \(IVIG\)](#)

[Intravenous Immune Globulin for the Treatment of Mucocutaneous Blistering Diseases \(NCD 250.3\)](#)

[Jevtana® \(Cabazitaxel\)](#)

[L-Dopa \(NCD 160.17\)](#)

[Lucentis® \(Ranibizumab\)](#)

[Photosensitive Drugs \(NCD 80.3\)](#)

[Self-Administered Drug\(s\) \(SAD\)](#)

[Vaccination \(Immunization\)](#)

[Verteporfin \(NCD 80.3.1\)](#)

[Vitamin B12 Injections to Strengthen Tendons, Ligaments, etc., of the Foot \(NCD 150.6\)](#)

[Xgeva®, Prolia® \(Denosumab\)](#)

[Zoledronic Acid \(Zometa® & Reclast®\)](#)

Other(s)

[NCCN Drugs & Biologics Compendium, National Comprehensive Cancer Network Website](#)

[Program Integrity Manual § 13.5.1 Reasonable and Necessary Provisions in LCDs, CMS Website](#)

[Thomson Micromedex DrugDex® Compendium, Micromedex Website](#)

Social Security Act (Title XVIII) Standard References, Sections:

- [1862\(a\)\(1\)\(A\) Medically Reasonable & Necessary](#)
- [1862\(a\)\(1\)\(D\) Investigational or Experimental](#)
- [1833\(e\) Incomplete Claim](#)
- [1861\(t\)\(1\) Drugs and Biologicals](#)

Guideline History/Revision Information

Revisions to this summary document do not in any way modify the requirement that services be provided and documented in accordance with the Medicare guidelines in effect on the date of service in question.

Date	Summary of Changes
04/01/2021	Template Update <ul style="list-style-type: none">• Reformatted policy; transferred content to new template
08/12/2020	Supporting Information <ul style="list-style-type: none">• Updated <i>References</i> section to reflect the most current information• Archived previous policy version MPG067.05

Purpose

The Medicare Advantage Policy Guideline documents are generally used to support UnitedHealthcare Medicare Advantage claims processing activities and facilitate providers' submission of accurate claims for the specified services. The document can be used as a guide to help determine applicable:

- Medicare coding or billing requirements, and/or
- Medical necessity coverage guidelines; including documentation requirements.

UnitedHealthcare follows Medicare guidelines such as NCDs, LCDs, LCAs, and other Medicare manuals for the purposes of determining coverage. It is expected providers retain or have access to appropriate documentation when requested to support coverage. Please utilize the links in the [References](#) section below to view the Medicare source materials used to develop this resource document. This document is not a replacement for the Medicare source materials that outline Medicare coverage requirements. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

Terms and Conditions

The Medicare Advantage Policy Guidelines are applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

These Policy Guidelines are provided for informational purposes, and do not constitute medical advice. Treating physicians and healthcare providers are solely responsible for determining what care to provide to their patients. Members should always consult their physician before making any decisions about medical care.

Benefit coverage for health services is determined by the member specific benefit plan document* and applicable laws that may require coverage for a specific service. The member specific benefit plan document identifies which services are covered, which are excluded, and which are subject to limitations. In the event of a conflict, the member specific benefit plan document supersedes the Medicare Advantage Policy Guidelines.

Medicare Advantage Policy Guidelines are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support UnitedHealthcare coverage decision making. UnitedHealthcare may modify these Policy Guidelines at any time by publishing a new version of the policy on this website. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the Medicare Advantage Policy Guidelines is believed to be accurate and current as of the date of publication and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

You are responsible for submission of accurate claims. Medicare Advantage Policy Guidelines are intended to ensure that coverage decisions are made accurately based on the code or codes that correctly describe the health care services provided. UnitedHealthcare Medicare Advantage Policy Guidelines use Current Procedural Terminology (CPT®), Centers for Medicare and Medicaid Services (CMS), or other coding guidelines. References to CPT® or other sources are for definitional purposes only and do not imply any right to reimbursement or guarantee claims payment.

Medicare Advantage Policy Guidelines are the property of UnitedHealthcare. Unauthorized copying, use, and distribution of this information are strictly prohibited.

*For more information on a specific member's benefit coverage, please call the customer service number on the back of the member ID card or refer to the [Administrative Guide](#).