World Trade Center (WTC) Health Program Medical Coverage Determination
Coverage of Off-Label Use of FDA-Approved Drugs
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I. Coverage Overview

This Medical Coverage Determination (MCD) outlines the coverage of medically necessary[1] off-label drugs[2] for WTC Health Program members.

Prescription drugs marketed in the United States must be approved by the U.S. Food and Drug Administration (FDA). FDA approval is based on the drug's demonstrated safety and effectiveness according to criteria specified by FDA regulations. Drug makers must also obtain FDA approval for the drug's labeling (i.e., package insert).[3] The drug label specifies the indication[4] for which a drug may be given and prescribing instructions, which include, but are not necessarily limited to, dosage, route of administration, duration, frequency of administration, and population to whom the drug would be administered.[5] When a provider prescribes a drug for a use other than the use specified in the labeling it is considered an "off-label drug use" (OLDU) or an "unapproved use."[6]

The WTC Health Program may provide coverage of OLDU if such use is considered medically necessary for the member's certified WTC-related health condition, or health condition medically associated with a certified WTC-related health condition. OLDU must be prescribed by a WTC Health Program provider[7] in accordance with the criteria set forth in this MCD.

II. Coverage Guidelines

The WTC Health Program may provide coverage of OLDU if the drug is approved for marketing by the FDA generally and the off-label use is supported by either the accepted compendia or other peer-reviewed literature accepted by the Program, as described below.

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[1] The WTC Health Program defines medically necessary treatment as the provision of healthcare services to manage, ameliorate, or cure a WTC-related health condition or health condition medically associated with a WTC-related health condition. *See* 42 C.F.R. § 88.1 at https://www.cdc.gov/wtc/regulations2.html.
[2] For purposes of this MCD, the term drug refers to human prescription drugs and biological drug products, as well as over-the-counter (OTC) drugs and OTC pharmacy products.
[3] *See generally* the term "Label" in the Drugs@FDA Glossary of Terms at https://www.fda.gov/drugs/drug-approvals-and-databases/drugsfda-glossary-terms.
[4] An indication is a diagnosis, illness, injury, syndrome, condition, or other clinical parameter for which a drug may be given. *See* Centers for Medicare & Medicaid Services Drugs and Biologicals, Coverage of, for Label and Off-Label Uses at https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?LCDId=33394&ContrId=275.
[5] *See* 21 U.S.C. § 321(k)-(n) for general requirements for drug labeling. *See also* 21 C.F.R. § 201.56 at https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-201/subpart-B/section-201.56.
[6] *See generally* the Agency for Healthcare Research and Quality (AHRQ) "Off-Label Drugs: What You Need to Know" at https://www.ahrq.gov/patients-consumers/patient-involvement/off-label-drug-usage.html.
[7] WTC Health Program providers must be affiliated with the Program provider network and agree to the Program's terms and conditions. The Program only covers formulary drugs prescribed by WTC Health Program providers.

A. WTC Health Program-Accepted Compendia

The WTC Health Program may provide coverage of OLDU that is supported by one or more of the compendia[8] listed below:

1. **American Hospital Formulary Service Drug Information (AHFS-DI)** – when the narrative text is supportive of off-label use.[9]

2. **Micromedex® DrugDex®** – when the off-label indication is Class I, Class IIa, or Class IIb.[10]

3. **Clinical Pharmacology** – OLDU is medically accepted when the off-label indication is supportive.[11]

4. **National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines©)** – when the off-label indication is Category 1 or 2A.[12]

   OR

5. **Lexi-Drugs®** – when the off-label indication is "Use: Off-Label" and rated "Evidence Level A."[13]

B. Other Acceptable Peer-Reviewed Literature

If the OLDU is <u>not</u> supported by one of the compendia listed above, the WTC Health Program may decide to provide coverage of OLDU that is supported by other peer-reviewed literature,[14] including peer-reviewed medical journal articles[15] and guidelines from national medical professional specialty organizations. [16]The peer-reviewed literature must demonstrate each of the following:

1. That the OLDU is adequately represented in the published evidence;

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[8] Drug compendia are summaries of drug information compiled by experts who have reviewed clinical data on drugs. The WTC Health Program follows those compendia accepted by the Centers for Medicare and Medicaid Services (CMS). *See* the Medicare Benefit Policy Manual, Chapter 15, Section 50.4.5 "Off-Label Use of Anti-Cancer Drugs and Biologicals" at https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/bp102c15.pdf.

[9] *See* AHFS-DI at http://www.ahfsdruginformation.com/ahfs-drug-information/.

[10] *See* Micromedex®, DRUGDEX® Detailed Drug Information, and Drug-Points® Summary Drug Information at https://www.micromedexsolutions.com/micromedex2/librarian/ssl/true.

[11] *See* Clinical Pharmacology at http://clinicalpharmacology.com/.

[12] *See* NCCN Guidelines at https://www.nccn.org/professionals/physician_gls/default.aspx.

[13] *See* LexiComp Online at https://online.lexi.com/lco/action/login.

[14] At a minimum, peer-reviewed medical journal articles must include at least two (2) clinical trials with reasonably large patient samples (e.g., 20-300) showing consistent safety and efficacy. Greater consideration will be given to higher-powered studies with levels of evidence in the following descending order: Randomized or nonrandomized controlled trials, prospective cohort studies, retrospective case-control studies, cross-sectional studies, surveillance studies, consecutive case series, and single case series. *See* CMS Drugs and Biologicals, Coverage of, for Label and Off-Label Uses at https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?LCDId=33394&ContrId=275.

[15] Note that the Program generally accepts peer-reviewed literature from the CMS list of acceptable publications found in the Medicare Benefit Policy Manual Chapter 15, Section 50.4.5 at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.

[16] Guidelines from national medical professional specialty organizations must be based on peer-reviewed science or published clinical guidelines from other federal agencies (e.g. Department of Veterans Affairs, TRICARE).

2. That the administered OLDU regimen (e.g., dosage, route of administration, length of treatment, etc.) is adequately represented in the published evidence;

3. That reported study outcomes of OLDU represent clinically meaningful outcomes experienced by the study population;

AND

4. That the study is appropriate to address the clinical question.

C. Insufficient Clinical Evidence to Support Authorization of OLDU

The following types of information are **insufficient** to meet the Program's requirements for peer-reviewed literature to support the authorization of OLDU:

1. Case reports and case series;[17]

2. Abstracts of conference proceedings or individual opinion/viewpoint articles;

3. Foreign language articles or publications;

4. Basic biomedical and pre-clinical research articles (e.g., animal studies, in vitro, ongoing experimental studies);

5. Anecdotal evidence or personal professional opinions from providers or groups of providers;

6. Supplement editions privately funded by parties with a vested interest in the recommendations of the authors;

AND

7. Provider or provider practice group recommendations to adopt a drug as their personal treatment/standard of choice.

III. Additional Criteria for OLDU Prescribers

In addition to the OLDU coverage criteria above, the WTC Health Program provider prescribing the OLDU must:

A. Be licensed under state law to prescribe the medication;

B. Prescribe the medication only to principally benefit the member and not for research purposes;

C. Have expert knowledge as a qualified professional[18] in the matter of the medically accepted indication and off-label drug use;

[17] Case reports or case series may be acceptable in limited situations where the indication for the treatment is extremely rare that other types of studies would not be possible; acceptability will be evaluated on a case-by-case basis.
[18] The Program considers a qualified professional to be an expert in the clinical indication for which OLDU is being prescribed. For example, an oncologist is considered a qualified professional for the purposes of prescribing OLDU for cancer treatment.

AND

D. Ensure an FDA-approved alternative is not available or appropriate (i.e., drug allergy, contraindication, etc.). If an FDA-approved alternative is available and is medically acceptable, the off-label medication should not be used.

IV. Prior Authorization Requirements

Medically necessary OLDU may require a prior authorization. Prior authorization requirements for drugs are listed on the WTC Health Program Pharmacy Formulary. Coverage of medically necessary OLDU is permitted only when in accordance with the WTC Health Program Formulary and other Program guidelines.[19]

For detailed prior authorization procedures, see instructions found in the WTC Health Program's Administrative Manual.[20] All documentation for completed prior authorization requests is subject to audit by the WTC Health Program.

[19] *See generally* WTC Health Program Administrative Manual for a full description of Program guidelines, policies, and procedures, at https://www.cdc.gov/wtc/ppm.html.
[20] *See* WTC Health Program Administrative Manual Chapter 12, Sections 3.5-6 at https://www.cdc.gov/wtc/ppm.html#pharmacy.