MEDICAL POLICY

POLICY TITLE	OFF-LABEL USE OF MEDICATIONS AND OTHER INTERVENTIONS
POLICY NUMBER	MP 2.103

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☐ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☒ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☐ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	**7/1/2024**

I. POLICY

Off-label use of a drug, biologic, device, or other intervention may be considered **medically necessary** when ALL of the following criteria are met:

- The drug, biologic or device is approved by the United States Food and Drug Administration (FDA); **and**
- There are no specific contraindications to proposed use for the specific member; **and**
- The off-label use is supported by at least **ONE** of the following:
  - Accepted standard of medical practice in the United States as evidenced by; **or**
    - Practice guidelines promulgated by a national medical or surgical specialty society; **or**
    - Expert medical opinion requested or identified by Capital; **or**
    - Peer-reviewed medical articles in major, authoritative clinical journals support proposed off-label use.
  - Category I or IIA indications in the NCCN Drugs and Biologics Compendium;**or**
  - Class I or IIA indication in the Thomson Micromedex ® DrugDex ®; **or**
  - Lexicomp/American Hospital Formulary System (AHFS-DI); **or**
  - Institute for Clinical and Economic Review; **or**
  - Blue Cross Blue Shield Association Evidence Street

If the FDA determines a drug, biologic, or device is contraindicated, or if the sources listed in this policy deem it to be not indicated or not recommended for specific conditions or defined groups of patients, those uses will be considered **investigational.**

Drugs, biologics, and devices that have not received FDA approval for any indication are considered **investigational** for all uses. Individual consideration of “off-label use” shall not include use of a drug, biologic, or device for treatment of a condition for which the FDA has determined the use to be contraindicated.

Note: For patients with late-stage metastatic disease (Stage IV), please refer to **MP 2.373** *Step Therapy Treatment in Cancer, Including Treatments for Stage Four, Advanced Metastatic Cancer, and Severe Related Health Conditions* for additional guidance.

Cross-reference:

MP 2.373 - Step Therapy Treatment in Cancer, Including Treatments for Stage Four, Advanced Metastatic Cancer, and Severe Related Health Conditions

II. PRODUCT VARIATIONS

TOP

This policy is only applicable to certain programs and products administered by Capital Blue Cross please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO –

Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies.

The FEP program dictates that all drugs, devices, or biological products approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational. Therefore, FDA-approved drugs, devices or biological products may be assessed on the basis of medical necessity.

Notes for Medicare Advantage:

1. Off-label use of FDA approved drugs and biologicals used in an anti-cancer chemotherapeutic regimen for medically accepted indications may be covered under Medicare if the indications are supported in either one or more Medicare recognized compendia or in peer-reviewed literature. Refer to Medicare Benefit Policy Manual (100-2, Chapter 15, Section 50.4.5- Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen) for the compendia list. *http://www.cms.gov/manuals/Downloads/bp102c15.pdf*
2. FDA approved drugs used for indications other than what is indicated on the FDA approved product label may be covered under Medicare if it is determined that the use is medically accepted, taking into consideration the Medicare recognized national drug compendia, authoritative medical literature and/or accepted standards of medical practice." Refer to Medicare Benefit Policy Manual (100-2, Chapter 15, Section 50.4.2- Unlabeled Use of Drug). *http://www.cms.gov/manuals/Downloads/bp102c15.pdf*

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III. DESCRIPTION/BACKGROUND TOP

The U.S. Food and Drug Administration (FDA) approves drugs and medical devices for specific indications. When a drug or device is used for indications other than those specifically documented in the labeling, it is referred to as an **off-label** use. Many off-label uses are effective, well documented in the peer-reviewed literature, and widely used.

IV. RATIONALE TOP

N/A

V. DEFINITIONS TOP

COMPENDIA is 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—

i. 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**.**
ii. Is indexed by drug or biological.
iii. Has a publicly transparent process for evaluating therapies and for identifying potential conflicts of interests.

OFF-LABEL USE The use of a prescription drug or medical device in the treatment of an illness or injury, which can include different dosing of a medication, for which it has not been specifically approved by the FDA.

VI. BENEFIT VARIATIONS TOP

The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits, and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER TOP

Capital Blue Cross' medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's

plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

***Specific Procedure Coding does not apply to this policy**

IX. REFERENCES

TOP

1. *Centers for Medicare and Medicaid Services (CMS) Medicare Benefit Policy Manual. Publication 100-02. Chapter 15. Section 50.4.2. Unlabelled Use of Drug. Effective 10/01/03. Accessed April 10, 2024.*
2. *Centers for Medicare and Medicaid Services (CMS) Medicare Benefit Policy Manual. Publication 100-02. Chapter 15. Section 50.4.5. Off-Label Use of Anti-Cancer Drugs and Biologicals. Accessed April 10, 2024.*
3. *National Comprehensive Cancer Network®. NCCN Drugs & Biologic Compendium™ (electronic version). Accessed April 10, 2024.*
4. *Radley DC, Finkelstein SN, Stafford RS. (2006). Off-label prescribing among office-based physicians. Arch Intern Med., 166(9), 1021-6.*
5. *Stafford RS. Regulating off-label drug use--rethinking the role of the FDA. N Engl J Med. 2008 Apr 3;358(14):1427-9.*
6. *IBM Micromedex® DrugDex® Compendium. Truven Health Analytics [Internet database]. Greenwood Village, CO. Accessed* April 6, 2023.
7. *American Hospital Formulary System (AHFS). Drug Information 2019. Accessed* April 10, 2024.
8. *Institute for Clinical and Economic Review (ICER). Accessed* April 10, 2024.
9. *Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Accessed* April 10, 2024.

X. POLICY HISTORY

TOP

MP 2.103	**04/10/2020 Administrative Update.** Note added for patients with late-stage metastatic disease (Stage IV), please refer to MP 2.373 Step Therapy Treatment in Cancer, Including Treatments for Stage Four, Advanced Metastatic Cancer, and Severe Related Health Conditions for additional guidance.

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	08/11/2020 Consensus Review. No change to policy statement. References reviewed.
	10/27/2021 Minor Review. Clarification and additional criteria coverage added. Background and references updated.
	08/26/2022 Minor Review. Orphan drugs transferred to new policy. Background and references updated.
	04/06/2023 Consensus Review. No change to policy statement. References updated
	04/10/2024 Consensus Review. No change to policy statement.

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