BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

BRAND OVER GENERIC MEDICATION EXCEPTION

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for BRAND OVER GENERIC MEDICATION EXCEPTION

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with a physician in the clinically appropriate specialty

Indication
- Diagnosis is consistent with the FDA approved product labeling

Age Requirement
- Age consistent with the FDA approved product labeling

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Baseline Clinical Evaluation

- Requested dosage, duration of use, and indication are consistent with FDA approved product labeling
- Experienced **ONE** of the following from the generic medication:
  - Therapeutic drug failure where expected drug effects did not occur after at least three months of use at usual therapeutic dose
  - Significant adverse drug reaction (intolerance or immune-related allergic reaction) rated Common Toxicity Criteria for Adverse Events (CTCAE) Grade 3 or higher, and determined to be probably or definitely caused by the generic medication

Brand Specific Criteria

- Tried an alternative generic medication from **THREE** different manufacturers or labelers (if available), and the significant adverse event recurred
- Prescriber submitted a report of the adverse reaction to MedWatch Form FDA 3500 – Voluntary Reporting at https://www.fda.gov/media/76299/download (copy of report required)

Safety

- No FDA-labeled contraindications
- No concomitant drug use that may cause severe adverse reactions or significant drug interactions requiring discontinuation

Additional Requirements

- No conflicting benefit exclusions

Documentation Requirements

- A completed request form must be submitted, including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration:

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualification

- Continues to be seen by a physician specializing in or in consultation with a physician in the clinically appropriate specialty

Clinical Response

- Condition has responded while on therapy, defined as no evidence of disease progression or unacceptable toxicity

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Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Provider submitted individual-specific clinical justification for why an A-rated generic medication cannot be used
- Tried an alternative generic medication from **THREE** different manufacturers or labelers (if available), and the significant adverse event recurred
- Prescriber submitted a report of the adverse reaction using MedWatch Form FDA 3500 – Voluntary Reporting (copy of report required)

Safety
- No concomitant drug use that may cause severe adverse reactions or significant drug interactions requiring discontinuation

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration:
- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

A generic drug is a medication made to be the same as an already marketed brand-name drug using the same active ingredient(s) as brand-name medicines, in the same dosage form, with the safety, strength, route of administration, quality, performance characteristics, and intended use. These similarities help to demonstrate bioequivalence, which means that a generic medicine works in the same way and provides the same clinical benefit as the brand-name medicine.

Generic products are A-rated by the Food and Drug Administration (FDA) for bioequivalence and therapeutic equivalence to the brand name product. An A-rated product will produce comparable absorption and blood levels to the brand name product. It is the judgment of the FDA that based on its determination of therapeutic

equivalence between generic and innovator (brand) drug products, those products evaluated as therapeutically equivalent can be expected to have equivalent clinical effect whether the product is brand name or generic drug product. The primary reference for therapeutic equivalence is found in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as "The Orange Book."

The Orange Book uses the first letter "A" to designate products that have demonstrated therapeutic equivalence. Those with a first letter "B" indicates products that have not. Products for which there are no known or suspected bioequivalence problems are rated as AA, AN, AO, AP, or AT, depending on the dosage form. These abbreviations are defined as follows: AA-conventional dosage forms; AN-solutions and powders for aerosolization; AO-injectable oil solutions; AP-aqueous solutions or intravenous non-aqueous solutions; AT-topical products. Products with actual or potential bioequivalence problems that have been resolved with adequate *in vivo* and/or *in vitro* evidence supporting bioequivalence are rated as AB. In some cases, the FDA recognizes more than one reference product. In these instances, a number is added to the end of the AB code (e.g., AB1, AB2, AB3, etc.). Products rated AB1 are bioequivalent to each other, products rated AB2 are bioequivalent to each other, and so forth.

The "Purple Book" is an easy-to-remember nickname for the "Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations." Biosimilar and interchangeable biological products will be listed under the reference product to which biosimilarity or interchangeability was demonstrated.

A "reference product" is the single biological product against which a proposed biological product is evaluated. Evaluations of biosimilarity and interchangeability for biological products are based on scientific and medical evaluations by FDA. FDA's determination that a product is biosimilar to a reference product or interchangeable with a reference product means that FDA has determined that the biological product meets the requirements for such products.

"Biosimilar" or "biosimilarity" means that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components, and there are no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency of the product.

An "interchangeable" biological product is a product that has been shown to be biosimilar to the reference product and can be expected to produce the same clinical result as the reference product in any given patient. To be determined to be an interchangeable biological product, it must be shown that for a biological product that is administered more than once to an individual the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.

MedWatch is the FDA's medical product safety reporting program. Health professionals, patients and consumers can use MedWatch to voluntarily report a serious adverse event, product quality problem, product use/medication error, or therapeutic inequivalence/failure that is suspected to be associated with the use of an FDA-regulated drug, biologic, medical device, dietary supplement or cosmetic. Form FDA 3500 – Voluntary Reporting at https://www.fda.gov/media/76299/download should be used to make such reports.

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FDA monitoring of post-market adverse events for **ALL** drug products (brand and generic drugs), is one aspect of the overall effort to evaluate the safety of drugs after approval. In most cases, reports of adverse events generally describe a known reaction to the active drug ingredient.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Form FDA 3500 – Voluntary Reporting at https://www.fda.gov/media/76299/download

Adverse drug reaction (ADR):
A potentially harmful, unintended effect caused by taking a medication. The National Cancer Institute (NCI) has established a standardized approach to measure the seriousness of an adverse event, known as the Common Toxicity Criteria for Adverse Events (CTCAE). Reactions are graded on a scale from 1 to 5.

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local, or noninvasive intervention indicated; limits age-appropriate instrumental activities of daily living (ADL= preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.)
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limits self-care ADL (bathing, dressing, and undressing, feeding self, using the toilet, taking medications, but not bedridden)
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to adverse event

Therapeutic Drug Failure:
Unable to accomplish the goal(s) of treatment where the expected drug effect(s) does not occur following a prescribed pharmacological treatment using therapeutic doses for at least 3-months
Drug Intolerance:
Using therapeutic dosing, the individual is unable to tolerate a known non-immune-mediated adverse effect(s) of a medication that is listed within the FDA product labeling; the reaction does not depend on prior exposure. The reaction may also be described as a drug side effect.

Drug Allergy or Drug Allergic Reaction:
An immune mediated reaction caused by taking a medication. A drug allergy is not the same as a drug intolerance or side effect. A drug allergy also is different from a drug toxic reaction which is caused by an overdose of a medication.

Resources:

Kesselheim AS, Misono AS, Lee JL, et al: Clinical Equivalence of Generic and Brand-Name Drugs Used in Cardiovascular Disease: A Systematic Review and Meta-analysis. JAMA 2008 December 3; 300(21): 2514–2526. doi:10.1001/jama.2008.758. Accessed February 22, 2023. Re-evaluated February 25, 2025.

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Davit BM, Nwakama PE, Buehler GJ, et al: Comparing Generic and Innovator Drugs: A Review of 12 Years of Bioequivalence Data from the United States Food and Drug Administration. Ann Pharmacother 2009 October; 43:1583-1597. Accessed February 22, 2023. Re-evaluated February 25, 2025.

Common Terminology Criteria for Adverse Events (CTCAE) version 5; published November 27, 2017; U.S. Department of Human Health Services, National Institute of Health, National Cancer Institute. Available at Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 – Myeloma Academy. Accessed March 04, 2023. Re-evaluated February 25, 2025.

Food and Drug Administration (FDA) Product Label available at U.S. Food and Drug Administration (fda.gov).

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.