Pharmacy Policy Bulletin

Title: Experimental/Investigational Use
Policy #: Rx.01.33

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (i.e., limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

**Intent:**
All prescription pharmaceutical agents available in the United States have FDA approved labeling. The label specifies which disease states a drug can be used to treat. However, use of a pharmaceutical agent may expand past the approved labeling and into what is known as off-label use. Coverage for off-label or experimental use will require Prior Authorization.

**Description:**
The US Food and Drug Administration (FDA) approves labeling that details all indications for which a pharmaceutical agent can be marketed. The approved indications identify the specific disease states that the agent has been shown to be safe, efficacious and meet all clinical requirements set forth by the FDA. An off-label or unlabeled use of a prescription drug or biologic is a use that has not been approved by the US Food and Drug Administration (FDA) and which is not identified in package labeling. Use of a drug for any indication, patient population, or route of administration other than those approved by the FDA and listed on the label or packaging insert is considered an off-label or unlabeled use.

Off-label use of prescription drugs and biologics not meeting the medical necessity criteria is considered experimental/investigational and may not be a covered by the prescription drug benefit.

In determining whether there is clinical evidence to support a medical necessity determination, FutureScripts will consider the quality of the published evidence as well as an assessment of the following information as submitted by the requesting physician.

Reliable evidence must demonstrate that the proposed off-label use for the specified medical condition is safe and effective and that the treatment’s beneficial effects outweigh its risks.
Policy:

Experimental and investigational uses are approved when ONE of the following inclusion criteria is met:

A. The narrative text in American Hospital Formulary Service--Drug Information (AHFS-DI®) is supportive of the use.
B. The indication is classified as Category 1 or 2A by National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium™.
C. The indication is classified as Class I or Class IIa in Micromedx®
D. Adequate published clinical research (supplied by the provider) as defined below

PUBLISHED CLINICAL RESEARCH

In order for an off-label use to be supported by published clinical research, all of the following criteria must be met:

A. The prescription drug or biologic must have been studied in at least two clinical trials conducted at different centers and the results must have been published in a national or international peer-reviewed journals with an editorial committee composed of physicians. Peer-reviewed medical literature includes scientific, medical, and pharmaceutical publications. It does not include in-house publications of pharmaceutical manufacturing companies or abstracts (including meeting abstracts).
B. A use is considered supported by clinical research when it appears in at least two Phase III clinical trials that have definitively demonstrated its safety and effectiveness as an appropriate medical treatment for the condition. If no Phase III trial evidence is available, at least two Phase II clinical trials with reasonably large patient samples showing consistent results of safety and efficacy may be considered in certain instances (e.g. rare diseases in which a Phase III study might be difficult to complete in a reasonable period of time after completion of the Phase II studies. Or when overwhelmingly good evidence of safety and effectiveness is noted in Phase II studies)

Reliable evidence must demonstrate that the proposed off label use for the specified medical condition is safe and effective and that the beneficial effects of the treatment outweigh its risks. In determining whether there is supportive clinical evidence for a particular use of a prescription drug or biologic, the Company considers the quality of the evidence in published, peer-reviewed medical literature. Among other things, such consideration involves the assessment of the following:

1. The prevalence and life history of the disease when evaluating the adequacy of the number of subjects and the response rate
2. The effect on the individual's well-being and other responses to therapy that indicate effectiveness (e.g. reduction in mortality, morbidity, and signs and symptoms)
3. Whether the clinical characteristics of the beneficiary and the indication are adequately represented in the published evidence
4. Whether the study is appropriate to address the clinical question, such as:
   a. If the study design is appropriate to address investigative questions (e.g. in some clinical studies, it may be unnecessary or not feasible to use randomized, double-blind trial, placebos, or crossover)
b. If non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.

c. Generally, case reports are considered uncontrolled, are based on anecdotal information, and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

5. The off-label use is supported by published clinical research and the results have been published in major, peer-reviewed medical journals such as, but not limited to:

<table>
<thead>
<tr>
<th>American Journal of Medicine</th>
<th>Gynecologic Oncology</th>
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<tbody>
<tr>
<td>American Journal of Psychiatry</td>
<td>International Journal of Radiation, Oncology, Biology and Physics</td>
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<tr>
<td>Annals of Internal Medicine</td>
<td>Journal of Clinical Oncology</td>
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<td>Annals of Oncology</td>
<td>Journal of Obstetrics and Gynecology</td>
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<td>Annals of Surgical Oncology</td>
<td>Journal of Pediatrics</td>
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<tr>
<td>Archives of Pediatric and Adolescent Medicine</td>
<td>Journal of the National Cancer Institute</td>
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<tr>
<td>Biology of Blood and Marrow Transplantation</td>
<td>Journal of the National Comprehensive Cancer Network (NCCN)</td>
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<tr>
<td>British Journal of Cancer</td>
<td>Journal of Urology</td>
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<td>British Journal of Hematology</td>
<td>Lancet</td>
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<td>British Journal of Medicine</td>
<td>Lancet Oncology</td>
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<td>Cancer</td>
<td>Leukemia</td>
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<td>Clinical Cancer Research</td>
<td>Pediatrics</td>
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<tr>
<td>Drugs</td>
<td>Radiation Oncology</td>
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<tr>
<td>European Journal of Cancer</td>
<td>The Journal of the American Medical Association</td>
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**EXPERIMENTAL/INVESTIGATIONAL**

Prescription drugs that are considered experimental/investigational are not covered because the safety and/or efficacy of the drug for those purposes cannot be established by a review of the available published peer reviewed literature. Prescription drugs and biologics are considered experimental/investigational for any of the following:

A. The prescription drug or biologic has not received FDA approval for any indication

B. The off-label use of the prescription drug or biologic does not meet the medical necessity criteria listed in this policy (i.e. the off-label use is not recognized by the appropriate compendia or published clinical research)

C. The FDA determined the prescription drug or biologic to be contraindicated for specific condition(s) or specific off-labels use(s)

D. The off-label use is not medically accepted or not indicated by a compendium for specific conditions (i.e. the indication is Category # in NCCN, Class III in Micromedex®) or when the narrative text in AHFS-DI® or Clinical Pharmacology® is not supportive

a. The absence of narrative text for an off-label use is considered neither supportive nor non-supportive

**REQUIRED DOCUMENTATION**
The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to records from the professional provider's office, hospital, nursing home, home health agency, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

**Black Box Warning:**

N/A

**Guidelines:**

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

**BENEFIT APPLICATION**

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

**References:**

N/A

**Applicable Drugs:**

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

This policy applies to all drugs that have clinical management policies addressing them.

**Cross References:**

NA

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**Policy Version Number:** 8.00

**P&T Approval Date:** July 13, 2017

**Policy Effective Date:** September 01, 2017

**Next Required Review Date:** July 13, 2018

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