Off-Label Drug Use
Medicare
Advantage

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<th>Line(s) of Business:</th>
<th>Original Effective Date:</th>
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<td>Medicare Advantage</td>
<td>05/08/2001</td>
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<td>Current Effective Date:</td>
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I. DESCRIPTION
The FDA approves drugs for specific medical indications, however, these approved drugs are often found to be effective for indications not approved by the FDA. The pharmaceutical companies frequently do not seek FDA approval for these "off-label" indications.

II. CRITERIA/GUIDELINES
A. Precertification is required for the off-label use of an FDA-approved drug when HMSA has a medical policy for that drug. Click for Medical Policies.
B. Drugs used for non-oncology-related off-label uses may be covered under Medicare if the carrier determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice.
   1. These decisions are made by the contractor on a case-by-case basis.
C. In the case of drugs used in an anti-cancer chemotherapeutic regimen, off-label uses are covered for a medically accepted indication as defined by the Medicare Benefit Policy Manual, Chapter 15, Section 50.4.5. Off-label, medically accepted indications are supported in either one or more of the compendia or in peer-reviewed medical literature.
   1. An off-label use will be considered as medically accepted when identified in one of the compendia listed below.
      a. Micromedex Drugdex evaluations when Strength of Recommendation is Class I, IIa or IIb
      b. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium and corresponding Clinical Practice Guidelines when Category of Evidence and Consensus is 1 or 2A
      c. Lexi-Drugs with Evidence Level A
      d. American Hospital Formulary Service Drug Information (AHFS-DI) with supportive narrative text
      e. Clinical Pharmacology with supportive narrative text
   2. A use is not medically accepted by a compendium if the:
      i. indication is a Category 3 in NCCN or a Class III in DrugDex; or,
      ii. narrative text in AHFS or Clinical Pharmacology is “not supportive,” or
      iii. indication is listed in Lexi-Drugs as “Use: Unsupported”

2. If the drug is not clearly stated to be effective for the off-label indication in one of the above compendia, the off-label indication must be supported by peer-reviewed medical literature.
3. Peer-reviewed medical literature may appear in scientific, medical, and pharmaceutical publications in which original manuscripts are published, only after having been critically reviewed for scientific accuracy, validity, and reliability by unbiased, independent experts prior to publication. In-house publications of entities whose business relates to the manufacture, sale, or distribution of pharmaceutical products are excluded from consideration. Abstracts (including meeting abstracts) are excluded from consideration.

4. In determining whether an off-label use is supported by the medical literature, the following will be considered:
   a. Whether the clinical characteristics of the beneficiary and the cancer are adequately represented in the published evidence
   b. Whether the administered chemotherapy regimen is adequately represented in the published evidence.
   c. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients.
   d. Whether the study is appropriate to address the clinical question, considering the following:
      i. Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover.);
      ii. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs; and,
      iii. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

5. Peer-reviewed medical literature will be used that appears in the regular editions of the following publications, not to include supplement editions privately funded by parties with a vested interest in the recommendations of the authors:
   a. American Journal of Medicine;
   b. Annals of Internal Medicine;
   c. Annals of Oncology;
   d. Annals of Surgical Oncology;
   e. Biology of Blood and Marrow Transplantation;
   f. Blood;
   g. Bone Marrow Transplantation;
   h. British Journal of Cancer;
   i. British Journal of Hematology;
   j. British Medical Journal;
   k. Cancer;
   l. Clinical Cancer Research;
   m. Drugs;
   n. European Journal of Cancer (formerly the European Journal of Cancer and Clinical Oncology);
   o. Gynecologic Oncology;
   p. International Journal of Radiation, Oncology, Biology, and Physics;
   q. The Journal of the American Medical Association;
   r. Journal of Clinical Oncology;
   s. Journal of the National Cancer Institute;
t. Journal of the National Comprehensive Cancer Network (NCCN);
u. Journal of Urology;
v. Lancet;
w. Lancet Oncology;
x. Leukemia;
y. The New England Journal of Medicine; or
z. Radiation Oncology

III. LIMITATIONS
If HMSA has a policy regarding the medical necessity of a specific drug, the request should be reviewed using that policy first. If the requested indication is not addressed in the specific policy, then the request will be reviewed using the Off-Label Drug Use policy.

IV. ADMINISTRATIVE GUIDELINES
A. Precertification is required for the off-label use of drugs for which HMSA has a medical policy including the policy Specialty Drugs Requiring Precertification. Click for Medical Policies.
B. To precertify, please complete the fax form as indicated.
C. The following must be submitted:
   1. Clinical information supporting the diagnosis
   2. Proposed treatment plan
   3. Published scientific literature or professional standards of care supporting the use of the drug for the requested off-label indication
D. Precertification is required for extension of treatment beyond the initial approval period.
   Current clinical documentation (e.g., office visit notes and applicable studies, supporting a response to treatment) must be submitted.

V. IMPORTANT REMINDER
The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that CVS/caremark reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VI. REFERENCES

Revised: August 2016