oscar

Clinical Guideline

Oscar Clinical Guideline: Approved and Accepted Off-label Medical Necessity Criteria for Products, Drugs and Biologicals (PG136, Ver. 2)

Approved and Accepted Off-label Medical Necessity Criteria for Products, Drugs and Biologicals

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

The Plan aims to ensure appropriate and safe use of FDA-approved/cleared prescription products (i.e., drugs, biologicals, devices) when used for medically accepted indications. Coverage may be provided⇅ when the product is used for:

- Indications listed in the FDA-approved/cleared labeling.
  ⇅*Please note: the Plan may deem an FDA-approved/cleared product to be unproven or not medically necessary if a review of published medical literature suggests the use may be unsafe or ineffective.*
- Off-label uses that are supported by sufficient evidence⇄ in medical compendia, evidence-based guideline or peer-reviewed literature:
  - Off-label usage may be considered reasonable and necessary if supported by sufficient evidence. However, off-label use is not covered if:
    - The use is identified by the FDA as not indicated.

- The use is specifically identified as not indicated in one or more of the compendia listed**.**
- Evidence-based guideline and/or peer-reviewed literature deems the use as not safe and/or effective.

⇄*Please note: For off-label use, the provider must submit documentation fully supporting the proposed use when requested. Coverage decisions will consider high quality published evidence.*

This policy provides coverage criteria for products requiring prior authorization that:

- Lack specific clinical guidelines or established criteria, including new products or those with recent major labeling changes***; or***
- Have been prescribed for an off-label indication.
    - Use must also be supported by high quality published evidence and not contradicted by other literature.

Please note: Other drug-specific or class-specific clinical guidelines may also be applicable. The Plan may review all requests made under the Medical or Pharmacy benefit against specific prior authorization criteria, as applicable and at its discretion.

Definitions

"**Biosimilar**" refers to copies of biologic drugs. They are similar to an FDA-approved biologic, known as the reference product.

"**Brand Name Drug**" means the first version of a particular medication to be developed or a medication that is sold under a pharmaceutical manufacturer's own registered trade name or trademark. The original manufacturer is granted a patent, which allows it to be the only company to make and sell the new drug for a certain number of years.

"**Compendia**" are summaries of drug information and medical evidence to support decision-making about the appropriate use of drugs and medical procedures. Examples include, but are not limited to:

1. American Hospital Formulary Service Drug Information
2. Elsevier Clinical Pharmacology
3. National Comprehensive Cancer Network Drugs and Biologics Compendium
4. Thomson Micromedex DrugDex
5. United States Pharmacopeia-National Formulary (USP-NF)

"**Documentation**" refers to written information, including but not limited to:

1. Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses;
2. Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"**Evidence-based, peer-reviewed medical journals**" are publications that publish original research and scholarly articles related to the medical field. These journals use a peer-review process in which submitted articles are reviewed by independent experts in the same field to ensure their scientific accuracy, validity, and reliability before publication. The articles published in these journals are often based on research that uses rigorous scientific methods to provide evidence for medical practices, therapies, and treatments. The goal of evidence-based medicine is to provide the most effective care to patients based on the best available scientific evidence.

"**FDA,**" or the Food and Drug Administration, is an agency of the United States federal government responsible for protecting and promoting public health through the regulation and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter medications, vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices, cosmetics, and veterinary products. The FDA's main goal is to ensure that these products are safe and effective for their intended use, and that their labeling and marketing are truthful and not misleading.

"**Formulary**" means a list of medications available to members with or without Prior Authorization.

"**Generic Drugs**" means prescription Drugs that have been determined by the Food and Drug Administration (FDA) to be equivalent to Brand Name Drugs, but are not made or sold under a registered trade name or trademark. Generic Drugs have the same active ingredients, meet the same FDA requirements for safety, purity, and potency and must be dispensed in the same dosage form (e.g., tablet, capsule, cream) as the Brand Name Drug.

"**High Strength/Quality Evidence**" is defined as at least one randomized, double-blind trial without significant limitations and with intent-to-treat analysis, confidence intervals reported, and consistent results from multiple trials or a meta-analysis with low heterogeneity. In some cancer-related cases, a non-blinded or single-blinded trial that meets the study objectives may also be considered as High Strength/Quality Evidence, such as in National Cancer Institute (NCI)-sponsored cooperative group studies or multicenter trials.

"**Low Strength/Quality Evidence**" is defined as evidence that includes observational studies, case reports, or case series, and in some cases, randomized clinical trials with significant limitations. It also encompasses evidence in the form of expert consensus panel reports or expert reviewer comments.

"**Moderate Strength/Quality Evidence**" is defined as at least one non-blinded or single-blinded, randomized or non-randomized clinical trial; a meta-analysis of randomized, controlled clinical trials with heterogeneous results if reasons for heterogeneity are adequately discussed; a randomized, controlled clinical trial with important methodological limitations; or inconsistent evidence from two or more randomized controlled trials with widely varying estimates of treatment effects. In some cancer-related cases, a non-blinded, non-randomized trial such as a phase II study may be considered as Moderate Strength/Quality Evidence for rare cancers or cancers with limited treatment options.

Medical Necessity Criteria for Initial Authorization

If there is no product-specific Clinical Guideline or indication-specific clinical criteria, the Plan considers the requested FDA-approved or cleared product medically necessary if **ALL** the following criteria are met:

1. The product is being prescribed by or in consultation with a specialist or clinician with relevant specialty training **IF** accurate diagnosis and prescription, determination of risks and benefits of treatment, dosing, monitoring for side effects, or overall care coordination require specialist training to ensure safe and effective use of the product***; AND***
2. The safety and effectiveness of use for the indication is consistent with **ONE** of the following⇶:
    a. FDA approved labeling (i.e., product information) for indication, including age, dosing (dosage, frequency, duration of therapy, and site of administration), and contraindications; ***or***
    b. Use is supported with an appropriate level of evidence of efficacy by at least **ONE** of the following compendia, and not contraindicated or otherwise not recommended in the FDA labeling:
        i. American Hospital Formulary Service-Drug Information (AHFS-DI) and Grades of Recommendation is **EITHER** "Recommended" **OR** "Reasonable Choice"***; or***
        ii. American Medical Association (AMA) Drug Evaluations, or its successor publication***; or***
        iii. Clinical Pharmacology and the off-label use carries a Strong Recommendation "For" use, with any level of evidence***; or***
        iv. Lexi-Drugs AND the indication is listed as "Use: Off-Label" **AND** rated as "Evidence Level A"***; or***

v. Micromedex DrugDex and the Strength of Recommendation for the indication is a Class I, Class IIa, or Class IIb***; or***

vi. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium and the level of evidence for the indication is Category 1, 2A, or 2B***; or***

c. Evidence-based, peer-reviewed, recognized medical literature meeting **ALL** of the following:

i. At least two articles from major peer-reviewed professional medical journals published in the United States or Great Britain have recognized, based on scientific or medical criteria, the product's safety and effectiveness for treatment of the indication for which the product has been prescribed***; and***

ii. No article from a major peer-reviewed professional medical journal has concluded, based on scientific or medical criteria, that the product is unsafe or ineffective or that the product's safety and effectiveness cannot be determined for the treatment of the indication for which the product has been prescribed***; and***

iii. The use is not listed as unsupported, not indicated, not recommended (or equivalent terms) in any of the medical reference compendia***; AND***

∃*Please note: the Plan may deem an FDA-approved/cleared product to be unproven or not medically necessary if a review of published medical literature suggests the use may be unsafe or ineffective.*

3. The member must have documented evidence of **ALL** of the following, if applicable:
   a. Failure of an adequate trial of at least three FDA-approved or cleared product (if available) that are considered the standard of care for the prescribed indication, unless:
      i. Clinically significant adverse effects are experienced***; or***
      ii. All FDA-approved or cleared alternatives are contraindicated***; or***
      iii. The request is for a product for treatment associated with cancer for a State with regulations against pre-requisite trial(s) of alternatives in certain oncology settings***; and***
   b. If the requested product is a Brand drug with a generic or biosimilar available, the member is unable to use or has tried and failed the corresponding generic or biosimilar product from two or more (≥ 2) manufacturers (if available)***; and***
   c. If the drug is to be used in combination with other drugs for a particular indication, the safety and efficacy of use of those drugs in combination must be supported by reliable evidence in peer-reviewed published medical literature***; AND***
4. The product being requested meets **BOTH** of the following:

a. The prescribed dose, frequency, duration of therapy, and site of administration are consistent with FDA-approved labeling, compendia of current literature, practice guidelines, or peer-reviewed literature for the relevant indication***; and***
b. If the requested dosage exceeds the Plan's quantity limit **AND** the prescribed dosage cannot be achieved using a different dose or formulation that is within the Plan's limit***; AND***

5. The member has no contraindications to the prescribed agent per FDA labeling***; AND***
6. Documentation (such as office chart notes, lab results or other clinical information) are provided for review to substantiate the above listed requirements.

If the above medical necessity criteria are met, the initial prior authorization (including duration) approval may be considered medically necessary when one of the following applies:

1. The duration of treatment requested is deemed medically necessary by the treating provider, when eligible for coverage per the member's benefits.
2. The initial prior authorization approval duration may be shortened or lengthened from the requested treatment duration in EITHER of the following cases:
    a. The nature of the service/treatment warrants a specific or different approval duration (e.g., 6-months, 12-months) based on the standards of care.
    b. The available clinical evidence or guideline recommendations support a specific approval period.

    NOTE: Benefit, eligibility, or other applicable Plan restrictions may impact the length of the authorization period.

    - *Ongoing prior authorization may be required after the initial approval period based on the service requested, clinical guidelines, and demonstration of continued medical necessity.*
    - *Prior authorization does not guarantee payment or assure coverage, which is contingent on the member's eligibility and available benefits. Concurrent review may be required during the approval period to monitor ongoing medical necessity and appropriate use.*
    - *Services must be delivered by plan-authorized providers and facilities, when applicable, and follow standards for evidence-based care delivery appropriate to the member's condition and goals of care.*

Medical Necessity Criteria for Reauthorization:

Prior authorization renewals will be reviewed on a case-by-case basis to determine medical necessity. Reauthorization requests will be considered medically necessary if **ALL** of the following criteria are met:

1. The member meets all applicable **Medical Necessity Criteria for Initial Authorization**, including:
    a. The prescribed use remains consistent with FDA-approved labeling or is supported by recognized compendia or high-quality published evidence***; and***
    b. The prescribed dose, frequency, duration of therapy, and site of administration remain consistent with FDA-approved labeling, nationally recognized compendia, or peer-reviewed medical literature for the relevant indication***; and***
    c. The member does not have any new contraindications to the prescribed product per FDA labeling***; AND***
2. The member has demonstrated a positive clinical response or benefit from therapy as evidenced by disease stability, disease improvement, or progress toward achievement of therapeutic goals as defined in the initial authorization***; AND***
3. The member has not experienced significant adverse effects, intolerable side effects, or unacceptable toxicity from the prescribed product that would necessitate discontinuation***; AND***
4. If the request is for a dose increase or change in dosing regimen, it must meet **BOTH** of the following criteria:
    a. The requested dosage, frequency, duration of therapy, and site of administration are supported by FDA-approved labeling, nationally recognized compendia, or peer-reviewed medical literature for the relevant indication (prescriber must submit supporting evidence)***; and***
    b. If the requested dosage exceeds the Plan's quantity limit **AND** the prescribed dosage cannot be achieved using a different dose or formulation that is within the Plan's limit.

Table 1: Level of Evidence Definitions

AHFS Grades of Recommendation	
Recommended (Accepted)	The drug or biologic should be used, is recommended/indicated, or is useful/effective/beneficial in most cases.
Reasonable Choice (Accepted, with Possible Conditions) (e.g., treatment option)	The drug or biologic is reasonable to use under certain conditions (e.g., in certain patient groups), can be useful/effective/beneficial, or is probably recommended or indicated.

Not Fully Established (Unclear Risk/Benefit, Equivocal Evidence, Inadequate Data and/or Experience)	Usefulness and/or effectiveness is unknown, unclear, or uncertain or is not well established relative to the standard of care.
Not Recommended (Unaccepted)	The drug or biologic is considered inappropriate, obsolete, or unproven; is not recommended, is not indicated, or is not useful/effective/beneficial; or may be harmful.
Elsevier Clinical Pharmacology (quality of evidence rating and strength of recommendation)	
Strong Recommendation	An off-label use that carries a Strong Recommendation "For" or "Against" use, with any level of evidence, should be considered binding and reflect that Elsevier recommends or does not recommend, respectively, the use of the drug for that indication in the situation described. All off-label uses with a strong level of recommendation will appear in the referential database and be clearly identified as recommended or not recommended; however, a strong recommendation "Against use" will not be found within the clinical decision support data.
Equivocal/Weak Recommendation	Off-label uses that have inconclusive data "For" or "Against" use carry a Weak Recommendation. A Weak recommendation, with any level of evidence, reflects a neutral or equivocal position (i.e., neither for or against use) by Elsevier. All off-label uses with a weak level of recommendation will appear in the referential database and be clearly identified as equivocal; however, a weak recommendation "Against use" will not be found within the clinical decision support data.
Lexi-Drugs Level of Evidence Scale	
A - Consistent evidence from well-performed randomized, controlled trials or overwhelming evidence of some other form (eg, results of the introduction of penicillin treatment) to support the off-label use. Further research is unlikely to change confidence in the estimate of benefit. B - Evidence from randomized, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate. C - Evidence from observational studies (eg, retrospective case series/reports providing significant impact on patient care), unsystematic clinical experience, or from potentially flawed randomized, controlled trials (eg, when limited options exist for condition). Any estimate of effect is uncertain.	

G - Use has been substantiated by inclusion in at least one evidence-based or consensus-based clinical practice guideline.	
Micromedex DrugDex Strength of Recommendation	
Class I - Recommended	The given test or treatment has been proven to be useful, and should be performed or administered.
Class IIa - Recommended, In Most Cases	The given test, or treatment is generally considered to be useful, and is indicated in most cases.
Class IIb - Recommended, In Some Cases	The given test, or treatment may be useful, and is indicated in some, but not most, cases.
Class III - Not Recommended	The given test, or treatment is not useful, and should be avoided.
Class Indeterminate	Evidence Inconclusive
NCCN Categories of Evidence and Consensus	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Table 2: Peer-reviewed Professional Medical Journals

NOTE: The list of medical journals provided as an example is not intended to be an all-inclusive or comprehensive list. Numerous other credible medical journals exist that are not included here, and this list should not be considered a complete representation of the medical journal landscape.

Journal Name	Specialty	Publisher
Academic Emergency Medicine	emergency medicine	Wiley-Blackwell
American Journal of Respiratory and Critical Care Medicine	respiratory and critical care	American Thoracic Society

Annals of Emergency Medicine	emergency medicine	Elsevier
Annals of Internal Medicine	internal medicine	American College of Physicians
Annals of Oncology	oncology	Elsevier
Annals of Surgery	surgery	Lippincott Williams & Wilkins
Annals of Surgical Oncology	oncology	Springer
Archives of Disease in Childhood	pediatrics	BMJ Group
Biology of Blood and Marrow Transplantation	hematology/Oncology	Elsevier
Blood	hematology	American Society of Hematology
BMJ Open	general medicine	BMJ Group
Bone Marrow Transplantation	hematology/Oncology	Springer Nature
British Journal of Cancer	oncology	Springer Nature
Cancer	oncology	Wiley
Circulation	cardiology	American Heart Association
Clinical Cancer Research	oncology	American Association for Cancer Research
Clinical Infectious Diseases	infectious diseases	Oxford University Press
Diabetes Care	diabetes	American Diabetes Association
Drugs	Pharmacology	Springer
Emerging Infectious Diseases	infectious diseases	Centers for Disease Control and Prevention
European Journal of Cancer (formerly the European Journal of Cancer and Clinical Oncology	oncology	Elsevier
Gastroenterology	gastroenterology	Elsevier

Gynecologic Oncology	gynecologic oncology	Elsevier
International Journal of Cancer	oncology	Wiley-Blackwell
International Journal of Radiation Oncology, Biology, Physics	radiation oncology	Elsevier
JAMA: The Journal of the American Medical Association	general medicine	American Medical Association
Journal of Clinical Oncology	oncology	American Society of Clinical Oncology
Journal of Neurology, Neurosurgery, and Psychiatry	neurology and psychiatry	BMJ Publishing Group
Journal of the National Cancer Institute	oncology	Oxford University Press
Journal of the National Comprehensive Cancer Network	oncology	NCCN
Leukemia	hematology/oncology	Nature
Nature	multidisciplinary sciences	Nature Publishing Group
Nature Communications	multidisciplinary sciences	Nature Publishing Group
Nature Medicine	general medicine	Nature Publishing Group
Neurology	neurology	American Academy of Neurology
Neuropharmacology	pharmacology	Elsevier
New England Journal of Medicine	general medicine	Massachusetts Medical Society
Obstetrics and Gynecology	obstetrics and gynecology	Wolters Kluwer
Pediatrics	pediatrics	American Academy of Pediatrics
PLOS One	multidisciplinary sciences	PLOS
Radiation Oncology	oncology	BioMed Central Ltd.

Stroke	neurology	American Heart Association
The American Journal of Clinical Dermatology	dermatology	Springer
The American Journal of Clinical Nutrition	nutrition	Oxford University Press
The American Journal of Gastroenterology	gastroenterology	Wolters Kluwer
The American Journal of Medicine	general medicine	Elsevier
The American Journal of Pathology	pathology	Elsevier
The American Journal of Physiology	physiology	American Physiological Society
The American Journal of Physiology - Endocrinology and Metabolism	physiology	American Physiological Society
The American Journal of Psychiatry	psychiatry	American Psychiatric Association
The American Journal of Sports Medicine	sports medicine	SAGE Publications
The American Journal of Transplantation	transplantation	Wiley-Blackwell
The Annals of Thoracic Surgery	thoracic surgery	Elsevier
The BMJ (formerly the British Medical Journal)	general medicine	BMJ Publishing Group
The British Journal of Haematology	hematology	Wiley-Blackwell
The British Journal of Psychiatry	psychiatry	Royal College of Psychiatrists
The British Journal of Surgery	surgery	Oxford University Press
The Cochrane Database of Systematic Reviews	evidence-based medicine	Wiley-Blackwell
The Journal of Adolescent Health	adolescent health	Elsevier
The Journal of Allergy and Clinical Immunology	allergy and immunology	Elsevier
The Journal of Bone and Joint Surgery	orthopedics	The Journal of Bone and Joint Surgery, Inc.

The Journal of Cerebral Blood Flow & Metabolism	neurology	SAGE Publications
The Journal of Clinical and Aesthetic Dermatology	dermatology	Matrix Medical Communications
The Journal of Clinical and Experimental Neuropsychology	neuropsychology	Taylor & Francis
The Journal of Clinical Endocrinology and Metabolism	endocrinology	Endocrine Society
The Journal of Clinical Hypertension	hypertension	Wiley-Blackwell
The Journal of Clinical Immunology	immunology	Springer
The Journal of Clinical Investigation	general medicine	American Society for Clinical Investigation
The Journal of Clinical Lipidology	lipidology	Elsevier
The Journal of Clinical Microbiology	microbiology	American Society for Microbiology
The Journal of Clinical Oncology	oncology	American Society of Clinical Oncology
The Journal of Clinical Pharmacology	pharmacology	Wiley-Blackwell
The Journal of Clinical Psychiatry	psychiatry	Physicians Postgraduate Press
The Journal of Clinical Psychology	clinical psychology	Wiley-Blackwell
The Journal of Clinical Sleep Medicine	sleep medicine	American Academy of Sleep Medicine
The Journal of Dental Research	dentistry	SAGE Publications
The Journal of Emergency Medicine	emergency medicine	Elsevier
The Journal of Geriatric Psychiatry and Neurology	geriatric psychiatry and neurology	SAGE Publications
The Journal of Hand Surgery	hand surgery	Elsevier
The Journal of Hospital Infection	infection control	Elsevier

The Journal of Hospital Medicine	hospital medicine	Wiley-Blackwell
The Journal of Infectious Diseases	infectious diseases	Oxford University Press
The Journal of Infectious Diseases and Therapy	infectious diseases	Springer
The Journal of Investigative Medicine	general medicine	BMJ Publishing Group
The Journal of Medical Internet Research	medical informatics	JMIR Publications
The Journal of Medical Microbiology	microbiology	Microbiology Society
The Journal of Neuroscience Nursing	neuroscience nursing	Lippincott Williams & Wilkins
The Journal of Neurosurgery	neurosurgery	American Association of Neurological Surgeons
The Journal of Nuclear Medicine	nuclear medicine	Society of Nuclear Medicine and Molecular Imaging
The Journal of Nuclear Medicine Technology	nuclear medicine	Society of Nuclear Medicine and Molecular Imaging
The Journal of Pathology	pathology	Wiley-Blackwell
The Journal of Rheumatology	rheumatology	The Journal of Rheumatology Publishing Company Limited
The Journal of the American Academy of Dermatology	dermatology	Elsevier
The Journal of the American Academy of Orthopaedic Surgeons	orthopedics	American Academy of Orthopaedic Surgeons
The Journal of the American Association of Nurse Practitioners	nursing	Wolters Kluwer
The Journal of the American College of Cardiology	cardiology	Elsevier
The Journal of the American College of Radiology	radiology	Elsevier
The Journal of the American College of Surgeons	surgery	American College of Surgeons
The Journal of the American Dental Association	dentistry	American Dental Association

The Journal of the American Heart Association	cardiology	Wiley-Blackwell
The Journal of the American Medical Directors Association	geriatric medicine	Elsevier
The Journal of the American Medical Informatics Association	medical informatics	Oxford University Press
The Journal of the American Optometric Association	optometry	American Optometric Association
The Journal of the American Podiatric Medical Association	podiatry	American Podiatric Medical Association
The Journal of the American Society of Hypertension	hypertension	Elsevier
The Journal of the American Society of Nephrology	nephrology	American Society of Nephrology
The Journal of the National Cancer Institute	oncology	Oxford University Press
The Journal of Thoracic and Cardiovascular Surgery	thoracic and cardiovascular surgery	Elsevier
The Journal of Thoracic Oncology	thoracic oncology	Elsevier
The Journal of Urology	urology	Elsevier
The Journal of Vascular and Interventional Radiology	interventional radiology	Elsevier
The Journal of Vascular Surgery	vascular surgery	Elsevier
The Lancet	general medicine	Elsevier
The Lancet Diabetes & Endocrinology	diabetes and endocrinology	Elsevier
The Lancet Haematology	hematology	Elsevier
The Lancet Infectious Diseases	infectious diseases	Elsevier
The Lancet Neurology	neurology	Elsevier
The Lancet Oncology	oncology	Elsevier

The Lancet Public Health	public health	Elsevier
The Lancet Respiratory Medicine	respiratory medicine	Elsevier

Experimental or Investigational / Not Medically Necessary

The use of products, drugs and biologicals are considered contraindicated, experimental, investigational, unproven, or not medically necessary in the following cases:

1. The product, drug, or biologic has not received approval or clearance for any indication from the U.S. Food and Drug Administration (FDA).
2. The prescribed use is listed as a contraindication in FDA labeling.
3. The Pharmacy and Therapeutics (P&T) Committee classifies it as experimental, investigational, or unproven because the safety and/or efficacy cannot be established after reviewing the published scientific literature.
4. Indications or diagnoses in which the product has been shown to be unsafe or ineffective.
5. Continued therapy for members who have developed an absolute contraindication, significant intolerance, or have failed to achieve the intended therapeutic outcome after an adequate trial of the product.
6. The prescribed use is not supported by any of the recognized compendia :
    a. AHFS-DI or Clinical Pharmacology: The narrative text is "not supportive" (or equivalent term).
    b. DrugDex: The level of evidence for the indication is Class III in DrugDex.
    c. Lexi-Drugs: Indication is listed as "Use: Unsupported."
    d. NCCN: The level of evidence for the indication is Category 3 in NCCN.
7. There is insufficient published evidence to support the safety and efficacy of the product for the prescribed use. Evidence is considered insufficient if it primarily consists of:
    a. Observational studies, case reports, or case series.
    b. Non-randomized studies or studies with serious methodological limitations.
    c. Expert consensus panel reports or expert reviewers' comments without supporting empirical evidence.
8. The prescribed use has been shown to be unsafe or ineffective in well-designed, controlled clinical trials or meta-analyses published in peer-reviewed medical journals.

References

1. American Academy of Family Physicians. (2017, Dec). Clinical Practice Guideline Manual. https://www.aafp.org/family-physician/patient-care/clinical-recommendations/cpg-manual.html#ix
2. American College of Physicians. (n.d.). www.acponline.org. Clinical Practice Guidelines and Recommendations. https://www.acponline.org/clinical-information/clinical-guidelines-recommendations
3. American Hospital Formulary Service - Drug Information (AHFS-DI). Available at: http://www.ahfsdruginformation.com
4. Bowling F, Badrick T. Methods for determining clinical utility. Clin Biochem. 2023 Nov;121-122:110674. doi: 10.1016/j.clinbiochem.2023.110674. Epub 2023 Oct 14. PMID: 37844681.
5. Clair JS. A New Model of Tracheostomy Care: Closing the Research–Practice Gap. In: Henriksen K, Battles JB, Marks ES, et al., editors. Advances in Patient Safety: From Research to Implementation (Volume 3: Implementation Issues). Rockville (MD): Agency for Healthcare Research and Quality (US); 2005 Feb. Table 1, AHRQ scale of research grades and levels. Available from: https://www.ncbi.nlm.nih.gov/books/NBK20542/table/A5857/
6. Elsevier Gold Standard Clinical Pharmacology Compendium (Clinical Pharmacology). EdElsevier Editorial Policy for Off-Label Data within Drug Information Products and Databases. Available at: https://www.elsevier.com/clinical-solutions/drug-information/editorial-policy/off-label-data
7. Halperin JL, Levine GN, Al-Khatib SM, et al. Further Evolution of the ACC/AHA Clinical Practice Guideline Recommendation Classification System, A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation, 2016;133:1426–1428. Doi: https://doi.org/10.1161/CIR.0000000000000312
8. Hayes, Inc. What is a Hayes Rating? https://evidence.hayesinc.com/static/HRating
9. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August 2023). Cochrane, 2023. Available from www.training.cochrane.org/handbook.
10. IBM® Micromedex® DRUGDEX®. IBM Watson Health. IBM Micromedex Policy on Compendia Drug Content. Available at: https://www.ibm.com/downloads/cas/GXNB3ZG4
11. Institute for Clinical and Economic Review, Peterson Health Technology Institute. (2023, Sept). ICER-PHTI Assessment Framework for Digital Health Technologies. https://phti.com/wp-content/uploads/sites/3/2023/09/ICER-PHTI-Assessment-Framework-for-Digital-Health-Technologies.pdf
12. Micromedex. Recommendation, Evidence and Efficacy Ratings. https://www.micromedexsolutions.com/micromedex2/librarian/CS/6FDB05/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/938DAC/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/evidencexpert.Int

ermediateToDocumentLink?docId=3198&contentSetId=50&title=Recommendation%2C+Evidence+and+Efficacy+Ratings&servicesTitle=Recommendation%2C+Evidence+and+Efficacy+Ratings

13. National Academies of Sciences, Engineering, and Medicine. 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press. https://doi.org/10.17226/13058.
14. National Comprehensive Cancer Network (NCCN). The NCCN Drugs and Biologics Compendium. NCCN Compendium®. Available at: https://www.nccn.org/compendia-templates/compendia/nccn-compendia
15. National Comprehensive Cancer Network. (n.d.). Development and Update of Guidelines. https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines
16. National Comprehensive Cancer Network. (n.d.). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) with NCCN Evidence Blocks™. https://www.nccn.org/guidelines/guidelines-with-evidence-blocks
17. National Institute for Health and Care Excellence. (2014, Oct). Developing NICE guidelines: the manual. Last updated: Nov 2023. https://www.nice.org.uk/process/pmg20/chapter/introduction
18. National Institute for Health and Care Excellence. (2014, Oct). Glossary. Last updated: Nov 2023. https://www.nice.org.uk/process/pmg20/chapter/glossary#randomised-controlled-trial
19. National Institute of Aging. (n.d.). NIA Glossary of Clinical Research Terms. https://www.nia.nih.gov/research/dgcg/nia-glossary-clinical-research-terms
20. National Institutes of Health. (April 2023). Glossary of Common Terms. https://www.nih.gov/health-information/nih-clinical-research-trials-you/glossary-common-terms
21. Schunemann HJ, Brennan S, Akl EA, Hultcrantz M, Alonso Coello P, Xia J, et al. The development methods of official GRADE articles and requirements for claiming the use of GRADE - a statement by the GRADE Guidance Group. J Clin Epidemiol. 2023 May 19;159:79-84. doi: 10.1016/j.jclinepi.2023.05.010.
22. The American College of Obstetricians and Gynecologists. (2021, Sep). Clinical Consensus Methodology. https://www.acog.org/clinical/clinical-guidance/clinical-consensus/articles/2021/09/clinical-consensus-methodology
23. U.S. Department of Health and Human Service Food and Drug Administration (FDA). Center for Drug Evaluation and Research | CDER. Available at: https://www.fda.gov/about-fda/fda-organization/center-drug-evaluation-and-research-cder.
24. U.S. Department of Health and Human Service Food and Drug Administration (FDA). Understanding Unapproved Use of Approved Drugs "Off Label". Available at: https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/understanding-unapproved-use-approved-drugs-label.

25. U.S. Food & Drug Administration. (2018, Jan). Step 3: Clinical Research. https://www.fda.gov/patients/drug-development-process/step-3-clinical-research
26. U.S. Food & Drug Administration. (2023, Dec). 510(k) Premarket Notification. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm
27. U.S. Food & Drug Administration. (2023, Dec). Device Classification Under Section 513(f)(2)(De Novo). https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm
28. U.S. Food & Drug Administration. (2023, Sept). In Vitro Diagnostics Emergency Use Authorizations (EUAs) - Serology and Other Adaptive Immune Response Tests for SARS-CoV-2. https://www.fda.gov/medical-devices/covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-emergency-use-authorizations-euas-serology-and-other-adaptive-immune-response
29. U.S. Food and Drug Administration (FDA). Off-label and investigational use of marketed drugs, biologics, and medical devices. Available at: https://www.fda.gov/regulatoryinformation/guidances/ucm126486.htm
30. U.S. Food and Drug Administration. Drugs@FDA. U.S. Department of Health & Human Services. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda.
31. U.S. Preventive Services Task Force. (2018, Oct). Grade Definitions. https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/grade-definitions
32. U.S. Preventive Services Task Force. (2022). A and B recommendations. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation-topics/uspstf-a-and-b-recommendations
33. U.S. Preventive Services Task Force. (n.d.). STANDARDS FOR GUIDELINE DEVELOPMENT. https://www.uspreventiveservicestaskforce.org/uspstf/sites/default/files/inline-files/standards-guideline-dev%20%281%29.pdf
34. Wolters Kluwer Lexi-Drugs®. Clinical Drug Information. Available at: http://www.wolterskluwercdi.com/lexicomp-online/

Clinical Guideline Revision / History Information

Original Date: 3/23/2023 Reviewed/Revised: 3/21/2024