ASHP Guidelines on the Evaluation of Off-Label Medication Use in the Inpatient Setting

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Purpose

The American Society of Health-System Pharmacists (ASHP) believes that, as medication experts, pharmacists serve an integral role in the effective management of off-label medication use. The responsibility for ensuring efficacious, safe, and cost-effective off-label medication use should be shared between providers and pharmacists with support from hospital or health-system leadership and the Pharmacy and Therapeutics (P&T) Committee. It is recommended to have policies and procedures in place to support the appropriate use of off-label medications. The purpose of these guidelines is to provide guidance to hospital and health-system pharmacists when navigating off-label medication use at any point during the medication-use process.

Note: This statement has not yet been published in the *American Journal of Health-System Pharmacy* (*AJHP*). Some minor editorial differences may exist between this document and the official one that will eventually appear in *AJHP*.

Definitions

Emergency Use Authorization (EUA): FDA may authorize unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biologic, radiologic or nuclear threat agents when certain criteria are met, including when there are no adequate, approved, and available alternatives.

Expanded Access: Also known as compassionate use; potential pathway for a patient with a serious or immediately life-threatening disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.

Off-label medication use: Any use outside of FDA-approved labeling, excluding investigational use, EUA, or expanded access

It is important to note that off-label medication use is a broad topic encompassing the use of older, relatively inexpensive medications for routine indications that have become standard of care, as well as the use of newer, expensive medications that are difficult to procure and have significant safety and monitoring parameters for non-FDA-approved indications. These guidelines aim to address off-label medication use in the inpatient setting in its entirety, with a focus on the various roles that pharmacists play in the process: direct patient care, formulary management, and overall safe and judicious use of medications.

Background

The Food and Drug Administration's (FDA) medication approval process is intended to ensure safe and efficacious use of medications in a studied population or disease state.[1] However, there are many scenarios in which healthcare providers prescribe FDA-approved medications for off-label uses, that is, for a use that is not approved by the FDA for that particular medication and subsequently not listed in the FDA-required medication labeling. Off-label medication use represents a therapeutic approach based on medical necessity, and may refer to use in unapproved indications, patient populations, dosing, dosage forms, or routes of administration.[1-2] See Table 1 for examples of common off-label medication use. These off-label uses frequently occur when a medication's labeling does not represent the most current therapeutic information, including data from recent clinical trials, published literature, or updated guidance from professional societies, often due to the financial and temporal constraints associated with the pharmaceutical company obtaining additional FDA approval.[2]

With off-label use, the medication is thought to be beneficial in the targeted population based on mechanism of action or supporting scientific literature.[2] The targeted populations are commonly vulnerable, special populations that are often excluded from clinical trials (i.e., pediatric, geriatric, pregnant, psychiatric patients, etc.), those with rare conditions in which treatment options are nonexistent or limited, or those with progressive or terminal diseases in

which appropriate alternatives have been exhausted. Available literature may include large, peer-reviewed studies, but may also be limited to single case reports, small case series, or retrospective cohort studies, potentially resulting in concern for inappropriate off-label use or subsequent harm.[3] As with all medication use, the risks and benefits of treatment with off-label use must be considered.[1]

Table 1: Examples of Off-Label Medication Use

Unapproved Use	Common Scenario
Unapproved disease states or conditions	Using an oncolytic agent only approved for use in one type of cancer in a patient with a different type of cancer
Unapproved populations	Using a medication only approved for use in adult patients in a pediatric patient
Unapproved frequencies	Using a medication only approved for use every eight weeks in a patient every four weeks
Unapproved dosages	Adjusting an approved adult dose for a pediatric patient
Unapproved dosage forms	Using a medication that is only approved for use as a capsule as a solution
Unapproved routes of administration	Use of a medication only approved for intravenous use for intravitreal use

Off-label medication use occurs frequently in both the inpatient and outpatient settings.[4] One study reported that off-label medication use accounts for up to 21% of outpatient prescribing, up to 23% of inpatient prescribing in adults, and up to 60% of prescribing in pediatric patients. The management in either setting varies largely due to reimbursement differences, approval pathways, and time constraints. In the inpatient setting, direct reimbursement for medications is not common, due to the Centers for Medicare and Medicaid Services' (CMS) prospective payment system with reimbursement based on diagnosis-related groups (DRGs). Approval for use is often governed by the healthcare team and the hospital's or health-system's corresponding policies and procedures. Treatment initiation is dependent on the approval workflow and procurement constraints. Conversely, in the outpatient setting, off-label medication use is tightly regulated by third party insurance plans through prior authorizations and upfront payment requirements. The pathway to approval and the timeline is governed by plan-specific criteria and requirements.

While FDA regulations establish guidance for safe and appropriate medication use, healthcare providers are not limited to FDA-approved labeling in their prescribing. As long as prescribers act in good faith with the best interest of the patient in mind and support their therapy decisions with "firm scientific rationale and sound medical evidence," off-label medication use

is acceptable and often deemed necessary.[2,5] Although seemingly similar in many ways, off-label medication use is not to be confused with investigational use, expanded access , or EUA.[5-7] The intent of using a medication off-label is to diagnose, prevent, or treat an individual patient for their condition, while investigational use aims to study a medication and contribute to generalizable knowledge. Expanded access and EUA may be considered a hybrid of the two, providing access to investigational therapies for patients meeting specific criteria with no suitable alternatives or in public health crises under the approval of FDA.[5,6]

Evaluation of Off-Label Medication Use by Direct Patient Care Pharmacists

When evaluating off-label medication use, the site of care must be considered due to inherent differences in the prevalence and urgency of off-label medication use. For example, institutions that treat patients with life-threatening conditions will require expedited evaluations for off-label medication use. Clinical practice areas with a high frequency of off-label drug usage include oncology, rare conditions, psychiatric, and pediatric practices.[8,9] Infusion and specialty medications given in the hospital setting intuitively require more extensive pharmacist oversight and involvement in the off-label process. Approval of off-label medication use in all settings will depend on evaluation of supporting literature, medication use policies, cost, and patient safety risks.

ASHP believes that pharmacists bear the responsibility for ensuring optimal patient outcomes and cost-effective care with drug therapies and should play a significant role in off-label medication use. When embedded in the patient care team, pharmacists critically evaluate medications for appropriate use on a case-by-case basis and can further escalate to the P&T Committee based on clinical judgement. As a valued member of the patient care team, pharmacists should have direct peer-to-peer discussions with physicians and the interprofessional team to address issues with off-label medication use and streamline the medication use workflow. Direct patient care pharmacists can also provide the P&T committee with the clinical information necessary to evaluate requests for off-label medication use to increase access to medications.

Decision-making process

During the order verification process, indications should be reviewed to monitor for off-label medication use and direct communication with the ordering provider is encouraged. The pharmacist evaluating the medication order for off-label use should check if the medication is available on the institution's formulary for ordering and purchasing, while also reviewing the supporting literature to evaluate the risk and benefits of its use. Other things to evaluate when reviewing an off-label medication order include: the original FDA-approved indication for the medication, the availability of other FDA-approved medications for the off-label indication, guidelines from professional societies, and the safety, financial, and operational implications of using the medication in an off-label manner. Medications that are not classified as formulary drugs, clinical trial drugs, or investigational drugs may not be stocked by the pharmacy.[10] If no available formulary alternatives exist or conditions are untreatable by existing formulary medications at the clinical discretion of the pharmacist and ordering provider, they can follow

the process for the institutions' non-formulary medication policy. If the off-label request is considered urgent and/or high cost, approval from each health-systems' designated point person (i.e. pharmacy director, attending physician, or P&T leadership) may be required based on individual clinical circumstances to expedite the request for off-label medication use.[4]

If the off-label medication request is for a non-formulary medication, the pharmacist should review the institution's interchange list for therapeutic alternatives and evaluate whether the medication meets the established criteria per the therapeutic interchange policy. Per ASHP, a therapeutic interchange protocol is the "authorized exchange" of therapeutic alternatives with similar chemical structure, efficacy, and safety profiles based upon guidelines, policies, and evidence-based protocols.[10] Therapeutic interchanges are often established to address drug shortage issues and maintain pharmacy budgetary restrictions. If a therapeutic interchange policy is already in place, the pharmacist could automatically change the prescribed medication to the preferred formulary alternative. The prescriber can be notified via the electronic health record or through a peer-to-peer discussion of the need to implement a therapeutic interchange for the originally prescribed medication. Education to the patient, nursing staff, and prescriber may be warranted to highlight the change and address any concerns with the therapeutic alternative. However, the prescriber or the patient may request to opt-out of the interchange process for various reasons such as the patient has been stabilized on the prescribed medication and it is now deemed medically necessary, the patient has a documented history of adverse effects to the formulary alternatives, treatment failures have resulted in the past while on the formulary alternatives, or there isn't a feasible, therapeutically-sound, formulary option.

If the patient meets any of the criteria to opt-out of the therapeutic interchange process, using a patient's own medication can be considered to address a non-formulary medication request for off-label use. Several advantages have been identified by using a patient's own medications to include maintaining the patient's usual course of therapy without interruption, perceived cost savings to the organization, enhanced medication compliance at discharge, and prevention of medication waste.[11] When considering the use of a patient's own medication, the pharmacist should refer to the institution's established policies and protocols. The hospital must first define in the policy when a patient's own medication can be used and that an order is required from the prescriber to indicate that the patient will utilize their own medication supply. The pharmacist must then coordinate with the patient or nurse to obtain the medication to identify and inspect for integrity per the patient's own medication protocol and ensure that medication is supplied in its original prescription bottle. The home medication will need to be supplied within a specified timeframe, usually within 24 hours. If the medication cannot be procured from the patient, alternative plans are coordinated with the prescriber, if the off-label medication use request is considered medically necessary or patient has been stabilized on the prescribed medication. Finally, if the nonformulary medication request for off-label use does not meet the criteria for a therapeutic interchange or the patient's own medication process, then the pharmacist can propose procuring the medication for urgent use while submitting an off-label medication request through the identified pathways. When the medication use

request has significant financial implications, consulting with a prior authorization specialist or transition of care pharmacist would be beneficial to ensure insurance coverage throughout the continuum of care.

If medications are high cost or have significant patient safety risks with limited supporting evidence, health-systems can consider the following pathways (See Figure 1) and form a collaborative committee of pharmacists, medical staff leaders/experts, risk management specialists and Institutional Review Board (IRB) representatives to review, collect data, and monitor off-label medication requests and use.[4,12] Off-label medication use requests should be made by the physician who will work jointly with pharmacists to review, evaluate, and grade the quality of supporting literature to determine the strength of the evidence and weigh the risks and benefits. Peer-review and evaluation of literature available can be performed by the P&T Committee. If there is a lack of sufficient supporting literature or high-quality evidence, a medication use evaluation (MUE) or IRB-approved study can be considered. A MUE is a tool for assessing a medication's use in a specific setting or patient population. The physician sponsor should help develop the proposal, ensure compliance with guidelines for off-label use, and collect and report efficacy and safety outcomes. Publication of results should be encouraged to share experience with off-label medication use to foster patient safety and increase quality of care. For any off-label medication request where there are limited efficacy data or safety concerns, patient informed consent is strongly recommended. Patients should be counseled on the rationale for off-label use, how it differentiates from standard recommendations, the known or anticipated risks and benefits, alternative options, and evidence or experience with off-label medication use. Any conflicts of interests should be disclosed and the patient discussion should be documented in the electronic health record. A systematic process for evaluating proposals for off-label medication use will reduce inappropriate use, increase patient safety, decrease risks to provider and patient, and encourage clinical research.

***Immediate Use of medications that are both off-label and outside of approved formulary criteria*[10]**

In the inpatient setting, formulary restrictions help to protect patients from inappropriate and unsafe off-label medication use. There should be a timely process to review the medical necessity of off-label medications that also deviate from institutional criteria to treat an individual patient (i.e. IVIG to treat myasthenia gravis). Immediate off-label medication requests that fall outside of the approved formulary restrictions and lack the appropriate evidence-based literature should undergo an additional peer review of medical necessity and an evaluation of patient safety (i.e. Anakinra for hemophagocytic lymphohistiocytosis). For routine off-label requests outside of approved formulary restrictions, a formal review by the P&T Committee should be considered (i.e. prazosin for PTSD).

Evaluation of Off-Label Medication Use by the Pharmacy and Therapeutics (P&T) Committee

Due to the varying strength and level of evidence, combined with patient acuity, decisions on off-label medication use requests should be reviewed by pharmacy in collaboration with key-stakeholders on a case-by-case basis through the institution's established process. When the

off-label medication or indication are requested to become part of the formulary due to routine utilization, a systematic formulary review and approval by an oversight committee, such as a P&T Committee, should be done to assess safety, efficacy, and cost-effectiveness. A P&T Committee is generally the medical staff committee managing of all aspects of medication use including formulary management and clinical policies and guidelines for a hospital or health-system.[10] P&T Committees are an interdisciplinary group that routinely evaluates safety, clinical efficacy, and cost effectiveness of medications, making them the most appropriate committee to review the evidence and determine if the benefits outweigh the risks.

When to consult P&T

While a majority of off-label medication use requests are handled on a case-by-case basis by the direct patient care pharmacist in collaboration with key-stakeholders, the P&T Committee may be consulted when there is:

- Desired routine use of an off-label therapy when the risk to the patient is determined to be significant or when evidence is poor
- Increased frequency of requests for the same off-label indication that are outside of the current standard of care
- Requests to expand formulary restrictions or criteria for use
- Requests to add a medication to formulary for an off-label indication
- Requests for off-label routes of administration
- Requests for electronic health record (EHR) product builds or customization
- High-cost medications where a financial review should be conducted
- Need for a drug class review to determine class effect and potential for therapeutic interchange

Frequently, off-label medication use requests are for rare or refractory indications or in patients where the medication has not been studied, such as pediatrics, neonates, elderly, or pregnant patients. Drug classes where common off-label use medications are used include anti-neoplastic, immunosuppressive, psychotropic, anti-inflammatory, and anti-rheumatic agents.[8,13] Off-label medication use requires incorporation of the non-formulary process institutions have developed. The available evidence and financial implications need to be evaluated prior to approval and utilization.

Each P&T Committee should develop a robust systematic approach for evaluating each off-label request, relying on the strength and grade of the scientific evidence to guide its decision.[14] Additional factors that need to be evaluated include the condition being treated, urgency of treatment, patient population, patient risk, cost effectiveness, and available therapeutic alternatives. The process must be flexible as each decision will be unique. P&T Committees may also form a collaborative subcommittee of experts to review an individual off-label medication use request or to monitor off-label use requests and collect retrospective data. The subcommittee should consist of medical staff leaders and experts, pharmacists, medication safety, ethics, IRB representatives, and risk management, at a minimum.

Determining the Quality and Strength of the Evidence[8,14,3]

A comprehensive and balanced assessment of the available evidence should be done for each off-label request and must be considered in the full context of the current standards of therapy. The P&T Committee may request a prescriber to provide supporting evidence of safety, efficacy and cost. The P&T Committee must then weigh both the quality and strength of the available evidence along with cost implications in making their final decisions.

The quality of evidence should directly link to both the health outcome and potential harm to the patient. The strongest evidence will come from well-designed, randomized, prospective clinical trials and inclusion in published national guidelines. Well-designed retrospective or case series will provide a moderate level of evidence and are stronger than individual case reports, and non-prospective trials warrant a closer review of the efficacy and safety. If a therapy is not supported by any published literature, the P&T Committee should consider this insufficient evidence to move forward with a request and may refer the requestor to the IRB or request that an MUE be completed. See Table 2 for a recommendation on grading the quality of evidence.

Table 2: Quality of Evidence[8,14,15]

LEVEL 1 **High level of evidence** (Prospective clinical trials with demonstrated health benefit, inclusion in national guidelines) **Low risk to patient** (Low incidence of ADRs, no significant safety concerns)	**LEVEL 2a** **Moderate level of evidence** (Retrospective clinical trials with sufficient sample size to establish health benefit, case series, inclusion in national guidelines) **Medium risk to patients** (Limited risk of ADRs, no or limited significant safety concerns)
LEVEL 2b **Low level of evidence** (Case reports, one case series, not included in national guidelines) **Medium risk to patients** (Limited risk of ADRs, some significant safety concerns)	**LEVEL 3** **Insufficient evidence** (no case series, case reports, clinical trials, or inclusion in national guidelines) **High risk to patients** (High incidence of safety concerns, significant safety concerns)

If an intervention consistently demonstrates both efficacy and safety, it should be considered to have a high strength of evidence. If the off-label request does not consistently show safety and efficacy, a closer determination of the risk vs. benefit is warranted. If neither efficacy nor safety is proven in the literature, the P&T Committee should consider this insufficient strength of evidence to move forward with a request. See Table 3 for a recommendation on grading the strength of evidence.

Table 3: Strength of Evidence[8,14,15]

HIGH Intervention is always efficacious and safe	**MODERATE** Intervention may be efficacious and safe
LOW Intervention is limited in efficacy or safety	**INSUFFICIENT** Efficacy and safety is not proven

Formulary management of off-label medication use

Formulary management includes selection of medications that optimize patient care, minimize costs, and improve outcomes while curbing inappropriate off-label use. Formularies may cover both inpatient and outpatient medication administration within a health-system. Formulary decisions are determined by considering the evidence, safety, economic, operational logistics, quality of life, social, and ethical factors. Additional information on formulary management concepts can be found in the ASHP guidelines on the pharmacy and therapeutics committee and the formulary system.[10] Formulary restrictions are one method P&T Committees use to impact prescribing, decrease adverse events, optimize patient outcomes, and reduce medication costs.[15] Restricting inpatient medications with potential safety risks, high costs, or limited therapeutic indications will help to ensure that each off-label request initiates a review process prior to the patient receiving it. A standardized list of drugs that have been routinely prescribed for off-label use can also be developed as an exception to the formal review process. When routine use of a medication falls outside of the P&T approved formulary restrictions or criteria for use, or lacks the appropriate evidence-based support, it should then undergo a formal review process including a peer-review of medical necessity and evaluation of potential safety concerns.

P&T Committee review

ASHP believes that the P&T Committee must ensure each decision is evidence-based, efficacious, safe, and cost-effective. Therapeutic benefit should never be assumed across every patient population. If a request for off-label medication use is supported by evidence that is graded as high-quality and strength, a P&T Committee can strongly consider approving the use. If there is a moderate quality of evidence and strength, the request can also be considered for formulary addition if there is a clear benefit-to-risk assessment. Any off-label request with low or insufficient evidence should be denied approval and be referred to the IRB or considered for an MUE. P&T Committees should develop criteria for use and establish a process for monitoring

ongoing efficacy and safety. It is also important to note that P&T Committees reserve the right to deny off-label use medication requests when they are not supported by the evidence, may harm the patient, or if they are not cost effective.

Conclusion

Off-label medication use has increased in frequency due to challenges associated with the medication's labeling remaining current with the constantly expanding body of literature. The decision to approve an off-label use of a medication, either at the direct patient care level or as an addition to the formulary, must be carefully evaluated to optimize patient outcomes, minimize patient safety risks, and ensure judicious use of resources. ASHP believes that pharmacists, as valued members of the patient care team, play an integral role in this off-label medication use process. As the medication experts, pharmacists provide valuable contributions to the systematic approach for critically evaluating off-label medication proposals based on evidence-based literature and supported by institutional policies. With the implementation of an off-label medication use policy or procedure incorporating these best practices guidelines, institutions will ensure optimal patient care while reducing potential uncertainties and risks.

Appendix A – Figure 1[4,12]

1. If sufficient high-quality evidence-based literature available and clear benefits outweigh the risks → Add to the formulary.
2. If evident support and rationale for off-label use but lack of sufficient evidence-base literature available → consider a MUE or proposal for use with appropriate medication dose and regimen, rationale for use, summary of relevant evidence, targeted populations, dispensing information to monitor its use based on set criteria and evaluate and collect data for efficacy and safety outcomes; and establish timelines for subsequent reporting of data collection and outcomes.
    - Time frame 1-3 months from proposal development to approval depending on frequency for expected use and risk and benefits; joint effort from P&T committee and physician sponsor for collection of outcomes data which can be prospective as part of the patient's medical care
    - If there is no clear benefit discontinue use of off-label medication
    - If request is considered "emergency use," require approval from P&T committee chair, pharmacy director and attending physician justified by individual clinical circumstances
3. If poor or limited evidence available → consider an IRB-approved research study.
4. Inappropriate or unsafe use → use not recommended.

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Additional information

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References

1. U.S. Food and Drug Administration. Understanding Unapproved Use of Approved Drugs "Off Label." www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/understanding-unapproved-use-approved-drugs-label (accessed 2024 Mar 20).
2. Wittich CM, Burkle CM, Lanier WL. Ten common questions (and their answers) about off-label drug use. *Mayo Clin Proc*. 2012; 87(10):982-990. doi:10.1016/j.mayocp.2012.04.017.
3. U.S. Department of Veterans Affairs. Center for Medication Safety. Pharmaceutical Use Outside of Approved Indications Guidance on "Off-label" Prescribing. www.pbm.va.gov/PBM/vacenterformedicationsafety/directive/GuidanceOffLabelPrescribing.pdf (accessed 2024 Apr 1).
4. Skledar SJ, Corman SL, Smitherman T. Addressing innovative off-label medication use at an academic center. *Am J Health Syst Pharm*. 2015;76(6):469-477.
5. U.S. Food and Drug Administration. "Off-Label" and Investigational Use of Marketed Drugs, Biologics, and Medical Devices. www.fda.gov/regulatory-information/search-fda-guidance-documents/label-and-investigational-use-marketed-drugs-biologics-and-medical-devices (accessed 2024 Apr 11).
6. U.S. Food and Drug Administration. Expanded Access: Information for Physicians. www.fda.gov/news-events/expanded-access/expanded-access-information-physicians#ExpandedAccess (accessed 2024 Mar 25).
7. U.S. Food and Drug Administration. Emergency Use Authorization. www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization (accessed 2024 Apr 11).
8. Dal Pan, GJ. Monitoring the safety of medicines used off-label. *Clin Pharmacol Ther.* 2012; 91: 787–795.
9. Kalis JA, Pence SJ, Mancini RS, et al. Prevalence of off-label use of oral oncolytics at a community cancer center. *J Oncol Pract.* 2015; 11(2): 139-43.
10. Ciccarello C, Leber, MB, Leonard MC, et al.. ASHP guidelines on the pharmacy and therapeutics committee and the formulary system. *Am J Health Syst Pharm*. 2021; 78(10):907-918.
11. Afana AH, Alhuthil R, Abdelwahab H, et al. Improve the process of patient's own medications dispensed from inpatient pharmacy: A single-center experience in Saudi Arabia. *J Clin Pharm* 2023;2:56-62.
12. Gazarian M, Kelly M, McPhee JR, et al. Off-label use of medicines: consensus recommendations for evaluating appropriateness. *Med J Aust*. 2006;185(10):544-548.
13. Blanco-Reina E, Muñoz-García A, Cárdenas-Aranzana MJ, et al. Assessment of off-label prescribing: profile, evidence and evolution. *Farm Hosp*. 2017;41(4):458-469.
14. Ansani NT, Fedutes-Henderson BA, Skledar SJ, et al. Practical approach to grading evidence for formulary recommendations. *Am J Health Syst Pharm*. 2005; 62(14):1498-1501.
15. Solano S, Dow J, Audley T, Bangalore N. Aligning formulary restrictions across a health system and improving access to and clarity of medication restrictions. *P&T*. 2019; 44(2):64-68.