

# ASHP Guidelines on the Pharmacy and Therapeutics Committee and the Formulary System

## Purpose

These guidelines outline the recommended processes and techniques for formulary system management and describe the pharmacist's responsibilities and roles in managing the formulary system in partnership with other health care professionals. These guidelines also provide assistance to pharmacists in the organization and operation of the pharmacy and therapeutics (P&T) committee or equivalent body, evaluation of medications for formularies, and development and implementation of strategies to manage medication use through the formulary system. A glossary of terms is provided in the appendix.

## Formulary and Formulary System

A *formulary* is a continually updated list of medications and related information, representing the clinical judgment of physicians, pharmacists, and other experts in the diagnosis, prophylaxis, or treatment of disease and promotion of health. A formulary includes, but is not limited to, a list of medications and medication-associated products or devices, medication-use policies, important ancillary drug information, decision-support tools, and organizational guidelines. A *formulary system* is the ongoing process through which a health care organization establishes policies regarding the use of drugs, therapies, and drug-related products and identifies those that are most medically appropriate and cost-effective to best serve the health interests of a given patient population.<sup>1</sup> Formulary systems are used in many different settings, including hospitals, acute care facilities, home care settings, and long-term-care facilities, as well as by payers such as Medicare, Medicaid, insurance companies, and managed care organizations. Many organizations have policy statements on the use of formularies.<sup>2–8</sup> This document focuses on the use of formulary systems in hospitals and health systems.

## Evolution of Formularies

Formulary systems have evolved over time. Modern formularies began as rudimentary drug lists developed by the military in the 1940s and came into more widespread use during the 1950s. Pharmacists, in conjunction with their organizations, developed policies to dispense generic equivalent drugs when a specific brand-name drug was prescribed. Protests from the National Pharmaceutical Council and the American Medical Association (AMA) resulted in state laws prohibiting this activity. Community pharmacies complied, but hospital pharmacies resisted. In the late 1950s, the ASHP minimum standard for pharmacies in hospitals called for the implementation of a formulary system.<sup>9</sup>

During the 1960s, the concept of a hospital formulary continued to grow. Hospitals developed policies that authorized pharmacists to make generic interchanges in an institutional formulary system based on prior consent from physicians.<sup>10</sup> ASHP and the American Hospital Association

(AHA) issued joint statements on the legality of formularies.<sup>11,12</sup> AMA and the American Pharmaceutical (later Pharmacists) Association subsequently joined with ASHP and AHA to revise the statements.<sup>13</sup> In 1965, two significant events occurred: (1) Medicare listed formularies as a reimbursement eligibility requirement<sup>14</sup> and (2) the Joint Commission on the Accreditation of Hospitals (now known as the Joint Commission) included an active P&T committee in its accreditation requirements.<sup>15</sup> Even with these actions, formularies were typically no more than lists of drugs stocked by the pharmacy.

By the 1980s, literature describing the clinical and economic value of well-designed formularies had emerged. Evidence from the hospital setting was published first, soon followed by evidence from the ambulatory care environment.<sup>10</sup> This literature led to more widespread acceptance of formularies. In 1986, the Pharmaceutical Research and Manufacturers Association officially accepted the concept of therapeutic interchange in hospitals and opposed its use in other settings.<sup>10</sup> As more evidence emerged, AMA's views on formularies for inpatient and outpatient settings became more closely aligned with those of ASHP. AMA's official policy on drug formularies and therapeutic interchange was first published in 1994<sup>16</sup> and has since been updated several times.<sup>5</sup>

Today, formulary systems are considered an essential tool for health care organizations. Formularies have grown from simple drug lists to comprehensive systems of medication-use policies intended to ensure safe, appropriate, and cost-effective use of pharmaceuticals in patient care.

## P&T Committee

The P&T committee is responsible for managing the formulary system. It is composed of actively practicing physicians, other prescribers, pharmacists, nurses, administrators, quality-improvement managers, and other health care professionals and staff who participate in the medication-use process. Customarily, P&T committee member appointments are based on guidance from the medical staff. The P&T committee should serve in an evaluative, educational, and advisory capacity to the medical staff and organizational administration in all matters pertaining to the use of medications (including investigational medications). The P&T committee should be responsible for overseeing policies and procedures related to all aspects of medication use within an institution. The P&T committee is responsible to the medical staff as a whole, and its recommendations are subject to approval by the organized medical staff as well as the administrative approval process. The P&T committee's organization and authority should be outlined in the organization's medical staff bylaws, medical staff rules and regulations, and other organizational policies as appropriate.

Other responsibilities of the P&T committee include medication-use evaluation (MUE), adverse-drug-event monitoring and reporting, medication-error prevention, and development of clinical care plans and guidelines. Information about these activities is available in ASHP guidelines on the topics.<sup>17–20</sup>

P&T committees have been credited with increasing practitioners' knowledge about drug therapy, improving the safety of drug therapy, and improving therapeutic outcomes.<sup>21</sup>

Consideration of patient care and unbiased reviews of the biomedical literature are the cornerstone principles of formulary decision-making. A conflict of interest (COI), financial or otherwise, may interfere with professionals' ability to make evidence-based decisions,<sup>22</sup> and even the appearance of a potential COI can undermine a formulary decision. The P&T committee has a responsibility to its patients and its organization to identify and address COI issues in its decision-making processes. Professionals participating in the P&T committee should disclose financial relationships with pharmaceutical manufacturers, medical supply vendors, other health care provider organizations, and other commercial interests. Some health care organizations exclude health care professionals with COIs from P&T committee membership, whereas others allow participation in committee discussions but prohibit voting on particular items. Practitioners requesting additions or changes to the formulary should disclose financial relationships with pharmaceutical companies and other potential COIs to the P&T committee.

Finally, the role of pharmaceutical company representatives and medical science liaisons in a health care organization should be carefully considered. Organizational guidelines should define appropriate relationships and interactions with such individuals. At a minimum, these guidelines should address the provision of pharmaceutical samples, indirect or direct funding support, and educational programming regarding formulary and nonformulary medications. Applications for formulary additions should be initiated and completed independently by the requesting health care provider and not by an industry representative or vendor. Refer to ASHP's "Guidelines on Pharmacists' Relationships with Industry" for more information on appropriate interactions with industry.<sup>23</sup>

## Managing the Formulary System

Health systems should develop, maintain, and implement a formulary management process. Decisions on the management of a formulary system should be founded on the evidence-based clinical, ethical, legal, social, philosophical, quality-of-life, safety, and economic factors that result in optimal patient care.<sup>24,25</sup> The process must include the active and direct involvement of physicians, pharmacists, and other appropriate health care professionals. This evidence-based process should not be based solely on economic factors. The formulary system should be standardized among components of integrated health systems when standardization leads to improved patient outcomes and safety.

Management of a formulary system is a significant component of a health care organization's ongoing medication-use policy development process. A comprehensive, well-maintained formulary that is tailored to the organization's patient care needs, policy framework, and medication-use systems ensures that the six critical processes identified by the Joint Commission (selection and procurement, storage, ordering and transcribing, preparing and dispensing, administration, and monitoring) work in concert to ensure optimal outcomes.<sup>26</sup> A well-managed formulary system ensures a close relationship among the organization's medication-use

policies, the therapies offered by the organization, and the medications routinely stocked in the pharmacy. A formulary also identifies those medications that are most medically appropriate and cost-effective to best serve the health interests of the health system's patient population. The P&T committee should interpret the term *medication* broadly in the context of care delivery to include alternative remedies (herbals and supplements), nonprescription drugs, blood derivatives, contrast media, and other diagnostic and treatment agents.<sup>26</sup>

The formulary system should include review and approval of all policies related to the medication-use process. All medication-use policies, regardless of their origination, should flow through the P&T committee. The organization's medical staff leadership (i.e., the body to which the P&T committee reports) should complete the final policy approval. Policy review and revision should occur as new information becomes available and at regularly established intervals (e.g., annually). Specific medication-use policies should address

- How medications are requested for addition to or deletion from the formulary,
- How medications are reviewed for addition to or deletion from the formulary, including who performs the reviews,
- The process for developing, implementing, and monitoring medication-use guidelines,
- Methods for ensuring the safe prescribing, distribution, administration, and monitoring of medications,
- Methods for selection of suitable manufacturers for specific medications (a pharmacist shall be responsible for specifications for the quality, quantity, and source of supply of all medications, chemicals, biologicals, and pharmaceutical preparations used in the diagnosis and treatment of patients),<sup>27</sup>
- The process for using nonformulary agents within the institution,
- The process for managing drug product shortages,
- The process for developing an organization-specific MUE plan,
- Policies regarding specific medication-use processes (e.g., procurement, prescribing, distribution, administration, monitoring), and
- The process for disseminating medication-use policies and how users will be educated regarding the process.

A formal process to review medication-use policies should be in place. This process may include the use of expert panels or subcommittees of the P&T committee. Expert panels should serve in an advisory role to the P&T committee, and their membership should include recognized experts in their areas of practice. Such panels can be helpful in applying clinical study results to specific patient populations, and panel members can help educate groups of physicians, who ultimately drive prescribing behaviors, about significant formulary changes. User groups, representing those primarily affected by the policy, may also be helpful. The P&T committee may also find subcommittees that address specific therapeutic areas to be beneficial (e.g., antimicrobial, cancer chemotherapy, cardiovascular, adverse-drug-reaction, or biotechnology subcommittees).

The P&T committee should have formal interactions (i.e., communication lines) with other committees whose functions may affect the medication-use process. These

committees would include those responsible for developing tools to facilitate medication use (e.g., forms or order set review committee, computerized prescriber-order-entry committee), those concerned with safety or performance improvement (e.g., quality-improvement or patient safety committees), those involved in developing patient care policies (e.g., medical and nursing committees), those involved with investigational medications (e.g., investigational review boards), and other committees whose actions may affect medication use (e.g., nutrition, equipment and supply, or finance committees). Recommendations from other committees, subcommittees of P&T, expert panels, and others should be submitted to the P&T committee for review. P&T committee decisions on recommendations should be communicated to the recommending group in a timely fashion.

### Evaluating Medications for Inclusion in the Formulary

The P&T committee should use a structured, evidence-based process in the evaluation of medications for formulary consideration. The P&T committee should be provided with information that reflects a thorough, accurate, and unbiased review and analysis of the evidence available in the scientific literature. The evaluation process should encourage objective consideration of clinical and care delivery information, facilitate communication, foster positive patient outcomes, and support safe and effective medication ordering, dispensing, administration, and monitoring. Decisions made by the P&T committee should support improved patient care outcomes across the continuum of care.

**Evidence-Based Evaluation.** Inclusion of a medication on a health system's formulary should reflect that an evidence-based evaluation of the relative merits and risks of the medication has been performed and that the institution's P&T committee, with input from appropriate experts, has determined that the medication is appropriate for routine use in the management of the patient population at that institution.

Evidence-based medicine is a systematic approach to the evaluation of biomedical literature and application to clinical practice and should be applied to formulary decision-making for medication product selection.<sup>24</sup> Evidence-based decision-making standardizes and improves the quality of patient care and promotes cost-effective prescribing.<sup>24,25</sup> To practice evidence-based medicine, practitioners must be proficient in retrieving, evaluating, and applying the biomedical literature to clinical practice.

Evidence-based decision-making incorporates the systematic approach to reviewing, evaluating, and applying the biomedical literature to guide formulary decisions. Various types and strengths of evidence (e.g., meta-analyses, randomized clinical trials, case reports, association consensus statements) may be useful in the decision-making process. Although different types of evidence are available for application, those with stronger evidence should be used to drive formulary decisions (e.g., meta-analyses, randomized controlled trials). Other types of evidence have a role in the decision-making process, however, and may be appropriate when stronger evidence is not available. Observational studies (i.e., case-control and cohort studies), case reports, and consensus opinions may be valuable even when stronger evidence is available. Some organizations find it useful to grade

evidence when evaluating formulary requests; several tools are available for this purpose.<sup>28–32</sup>

Published evidence and expert opinion are not the only resources available to aid in the formulary decision-making process. Internal data and prescribing and outcomes information may be helpful in formulary decision-making. When published data are not available, it may be appropriate to incorporate expert opinion into the review process. Experts in practice areas sometimes have access to unpublished data or reports that may offer insight into difficult formulary decisions.

The P&T committee should use formulary packets and dossiers prepared by pharmaceutical manufacturers with the utmost caution, since the objectivity of these documents may be challenged. The formulary decision-making process should instead be guided by an independent review of evidence published in the biomedical literature, application of expert opinion, and use of internal data and benchmarking programs.

The information should be provided to the P&T committee in a written document with a standard format (e.g., a drug monograph, drug review, drug-evaluation document). All information provided in the drug-evaluation document should be referenced to the evidence or identified as a conclusion supported by evidence. Any areas of consensus recommendations or opinion should be clearly identified.

**Types of Drug Reviews.** There are four major types of drug reviews: new drug monographs, reevaluations of previous formulary decisions, therapeutic class reviews, and expedited reviews of newly approved medications. Because of the expertise and training of pharmacists (drug information specialists in particular), pharmacists should play an integral part in the preparation and presentation of the drug review document to the P&T committee.

**New drug monographs.** When the Food and Drug Administration (FDA) approves a new drug for marketing that is relevant to the health system, a drug monograph should be prepared for formulary consideration by the P&T committee. New chemical entities warrant a thorough evaluation and a written drug monograph. A short (e.g., one-page) summary could be provided along with the full monograph.<sup>33</sup> Some organizations use an executive summary format. A new drug that is significantly similar to other available therapeutic alternatives may be presented in a more abbreviated manner (e.g., an abbreviated monograph) provided that the P&T committee or experts agree that the drug is therapeutically equivalent to agents already available on the formulary.

**Addenda to original monographs used to reevaluate previous formulary decisions.** Formulary decisions may need to be reassessed based on relevant new information or in light of newly marketed drugs or dosage forms. New data on safety, efficacy, stability, methods of administration, cost, or pharmacoeconomics may warrant a reevaluation of the drug or dosage strengths or formulations stocked by the health system. An addendum to the original monograph summarizing the new information should be developed for evaluation by the P&T committee. The P&T committee may want to establish reassessment dates at the time of formulary review so that the committee can reassess the effect of a formulary decision on quality or cost of care.

**Therapeutic class reviews.** Review of an entire therapeutic class of drugs should be performed at regular intervals, which may be determined by the P&T committee or

influenced by regulatory agencies. A therapeutic class review should include all formulary and nonformulary medications within the class and may include institutional utilization or outcomes data and newly published information. Therapeutic class reviews may lead to formulary removal of therapeutically equivalent drugs or a change in restriction or guideline status for a drug.

*Expedited reviews.* A process should be available for the P&T committee to conduct an expedited review of a new drug, new indication for a drug, or reevaluation of a previous formulary decision. Criteria should be in place to describe when an expedited review is warranted. For example, approval of a new chemical entity for a disease with no therapeutic alternative may warrant an expedited review to ensure availability of the drug for patients who need it. Likewise, a significant new safety concern may warrant an expedited review for addition of restrictions or removal from the formulary.

**Elements of a Drug-Evaluation Document.** The drug-evaluation document should present the evidence in a manner that is thorough, is consistent from medication to medication, and provides all necessary facts and analysis to the P&T committee to allow for an informed formulary decision. Document structure may vary, depending on the needs of the specific health system and P&T committee, but the following elements are essential to all such documents:

- Brand and generic names and synonyms,
- FDA approval information, including date and FDA rating,
- Pharmacology and mechanism of action,
- FDA-approved indications,
- Potential non-FDA-approved (off-label) uses,
- Dosage forms and storage,
- Recommended dosage regimens,
- Pharmacokinetic considerations,
- Use in special populations (e.g., children, elderly, patients with renal or liver failure),
- Pregnancy category and use during breast-feeding,
- Comparisons of the drug's efficacy, safety, convenience, and costs with those of therapeutic alternatives (with evidence tables when feasible),
- If information on comparative efficacy is minimal or lacking, data on absolute efficacy (i.e., efficacy versus placebo),
- Clinical trial analysis and critique,
- Medication safety assessment and recommendations (adverse drug reactions; drug–drug and drug–food interactions; specific therapy monitoring requirements; unusual administration, storage, or stability issues; and potential for medication errors, such as look-alike or sound-alike issues), and
- Financial analysis, including pharmacoeconomic assessments.

Formulary status recommendations (e.g., from drug information services or expert groups) may be included in the drug evaluation document. In some organizations, recommendations are not provided in the written document in order to promote an unbiased discussion by the P&T committee. Recommendations should consider the formulary status (addition or rejection) of a medication, as well as the need for restrictions, educational efforts, or policies and procedures to ensure safe and appropriate use within the health system.

**Pharmacoeconomic Assessments.** Rigorous pharmacoeconomic evaluations can and should be conducted in some cases when reviewing new medications. These evaluations should explicitly state the perspective of the analysis (e.g., patient, health care provider, payer) and should include consideration of all costs and consequences relevant to that perspective. When new medications being considered are found to be therapeutically equivalent to existing alternatives (having equivalent efficacy and safety), then the cost-minimization approach is appropriate. In these circumstances, it is important to consider costs associated with the medication and nonmedication-related costs (e.g., costs of administration, monitoring, prolonged hospital stay, and laboratory test monitoring; costs to patients and providers).

While cost-effectiveness analysis (evaluating the incremental difference in investment necessary to produce an incremental difference in clinical outcome) is another potentially useful analytic approach, it is not often used for formulary decision-making because of its complexity and need for strong evidence or data. The academic value of this approach lies in its ability to show how little (or how much) must be spent to achieve a particular margin of clinical advantage when comparing an alternative that is more expensive but safer or more efficacious. No standards currently exist to determine how much money is reasonable to spend for any given improvement in outcome; however, it is unreasonable to recommend alternatives of lower quality simply to achieve cost savings. This approach can be used to demonstrate how a decrease in clinical outcomes associated with the use of a less expensive agent can be offset by investing the savings achieved in other interventions that produce even greater total benefits.

Cost-utility evaluations (evaluating the incremental difference in investment necessary to produce an incremental difference in quality-of-life-adjusted clinical outcome [e.g., incremental cost per quality-adjusted life years gained for one medication versus another]) may also be beneficial by serving to reflect patient preference in formulary decision-making. However, the same concerns related to the use of cost-effectiveness evaluations apply to this approach.<sup>34–36</sup>

Decision analysis models incorporating local data can be employed when published pharmacoeconomic data are limited or unavailable. Probabilities for each outcome can be extracted from the published literature or drawn from local data sources, which would provide a more relevant local perspective on outcomes. Costs associated with medications and outcomes should reflect those of the health care system.

Pharmacoeconomic analyses published in the medical literature or provided in the manufacturer's formulary dossier should be analyzed carefully before being included as part of the review process. Particular attention should be paid to the assumptions made in these studies. In many situations, assumptions made to simplify economic studies are not valid in particular institutions. Institution-specific costs are often different from the costs used in published studies, and local data should be used when incorporating their results into medication reviews.<sup>37,38</sup>

Even if a formal pharmacoeconomic evaluation is not included in a drug review document, a financial evaluation must be conducted, including consideration of nonmedication-related costs and financial consequences to the pharmacy and to the organization as a whole.

**Formulary Exceptions.** Exclusion of a medication from a formulary may affect coverage of and access to the medication. In a closed formulary system, for example, only medications listed on the formulary are covered under the patient's drug benefit. Regardless of health-system setting, the formulary system should include an exception process that provides prescribers and patients with timely access to medications that are not on the formulary but are medically necessary for the care of the patient. The underlying principle for such a process is that unique patient needs may not be satisfied by use of the formulary medications. The formulary exception process should generate information on nonformulary medication use that will enable the P&T committee to evaluate trends in such use. Criteria for approval of nonformulary medications should be developed (e.g., allergy to or therapeutic failure of formulary alternative, condition not treatable by formulary medications).

**Subformularies.** Depending on state regulations, subformularies may be developed and maintained, using the same evidence-based process, to provide lists of appropriate and approved medications for furnishing by nonphysician providers or to specific patient subsets, such as Medicare patients. Health systems must follow specific rules and regulations provided under the U.S. Medicare Modernization Act of 2003 in their evaluation and inclusion of medications in a Medicare formulary for those medications to be covered.<sup>39</sup>

## Strategies for Managing Medication Use

Common strategies for managing medication use via the formulary include use of generic drugs, therapeutic interchange, guided-use policies, clinical practice guidelines, and policies for off-label prescribing and the use of research pharmaceuticals. MUE is also important in managing medication use.

**Generic Drugs.** Optimizing the number of medication entities and products available from the pharmacy can produce substantial patient care and financial benefits. These benefits are greatly increased through the use of generic equivalents (drugs considered bioequivalent by FDA [i.e., AB-rated drug products<sup>40</sup>] and therapeutic equivalents [drug products differing in composition or in their basic drug entity that are considered to have very similar pharmacologic and therapeutic activities]). The use of high-quality generic equivalents is encouraged in order to provide the best possible care at an affordable cost. Use of generic drugs that have been deemed bioequivalent by FDA does not require review or approval by the P&T committee, although a review of all new medications for key safety issues (e.g., look-alike, sound-alike concerns) should be conducted to prevent medication errors. For some drug categories, such as those with a narrow therapeutic range, a more thorough evaluation of the bioequivalency data and approval of experts or the P&T committee should be considered before implementing a generic substitution.

The P&T committee must establish policies and procedures governing the dispensing of generic equivalents. These policies and procedures should include the following points:

- The pharmacist is responsible for selecting from available generic equivalents those drugs to be dispensed pursuant to a prescriber's order for a particular medication.
- The prescriber has the option, at the time of prescribing, to specify the brand or supplier of the drug to be dispensed for that particular medication order if considered clinically justified.
- The prescriber's decision should be based on pharmacologic or therapeutic considerations (or both) relative to that patient.

**Therapeutic Interchange.** Therapeutic interchange is the authorized exchange of therapeutic alternatives in accordance with previously established and approved written guidelines, policies, or protocols within a formulary system.<sup>1</sup> Therapeutic interchange provides pharmacists with the authorization to use a formulary therapeutic alternative in place of a nonformulary medication or a non-preferred formulary medication without having to contact the prescriber. Drugs appropriate for therapeutic interchange are drug products with different chemical structures that are expected to have similar therapeutic effects and safety profiles when administered to patients in therapeutically equivalent doses. The authorization of a therapeutic interchange and notification of the prescriber should occur according to the organization's policy. In some organizations, prescribers agree to the therapeutic interchange process as part of their overall agreement to follow the organization's policies when they are granted prescribing privileges. Other organizations require that the prescriber be notified each time a medication is interchanged. A process should be established for when the prescriber wishes to opt out of the interchange. Adequate educational initiatives should be undertaken to ensure that everyone affected (prescribers, patients, pharmacists, nurses, and other health care professionals) is notified of the therapeutic interchange. Guidelines on therapeutic interchange are available elsewhere.<sup>41</sup>

**Guided-Use Strategies.** Medications may be added to the formulary with additional processes in place to guide the use of the medications to improve therapeutic outcomes, prevent adverse events, or reduce costs. Examples of strategies to help guide the use of medications in addition to therapeutic interchange may include the following.

**Established-use criteria.** Patients must meet the established criteria before the medication is dispensed. A process should be developed to cover situations in which the patient does not meet the established criteria, but the medication is nevertheless determined to be medically necessary. This strategy may also be useful when medications are in short supply.

**Restricting drug use to a service.** A specific service must approve the use of the drug before dispensing. This strategy can be used when inappropriate use or severe adverse effects may occur, and it can also be employed for antimicrobial agents when inappropriate use or overuse can result in resistant organisms and pose a danger to the general patient population or the public.

**Limiting use of the drug to specially trained individuals.** This strategy may be appropriate when the drug is inherently dangerous and should only be used by individuals with specific training (e.g., restricting use of chemotherapy agents to oncologists).

**Designating medications for use in specific areas.** Such policies can be helpful when administration of a medication requires special equipment or staff with particular skills to use the medication safely (e.g., limiting neuromuscular blockers to operating rooms and critical care areas).

*Approval of medical director (or designee) before drug use.* This strategy is particularly appropriate when the P&T committee has reviewed a high-cost medication and determined that the drug has little or no role in the care of patients at that organization but a prescriber would like to use the medication on a nonformulary basis.

**Clinical Practice Guidelines.** The implementation of medication-use policy decisions is a complicated process that, when properly conducted, can decrease variability in practice and improve patient outcomes, including clinical and economic consequences of care. Many tools are used to reduce practice variability, reduce cost, and improve quality, including order sets, clinical pathways, treatment algorithms, and clinical practice guidelines. While active intervention tools, such as order sets, directly influence prescribing for individual patients, clinical practice guidelines influence prescriber behavior in a passive manner, primarily through education. Like the medication formulary, clinical practice guidelines should reflect current biomedical evidence, although they may also include expert opinion of prescribers within a practice setting. Clinical practice guidelines are developed and disseminated by national and international organizations, but they can also be developed locally. Not all guidelines are equally valuable, however. Policymakers should not assume that guidelines, even those endorsed by respected organizations, are necessarily evidence based and should carefully review guidelines to ensure that they are truly evidence driven and current. Regardless of the source of the synthesis of biomedical evidence that forms the framework for an individual guideline, a locally conducted consensus development process, incorporating local expertise, must be performed if a guideline is to be accepted and followed.

Whether the medication formulary is a reflection of existing clinical practice guidelines in a particular organization or vice versa, it is critical that the guidelines and formulary are consistent. If a specific medication is recommended by a clinical practice guideline, it should in the majority of cases be on the formulary. As formulary changes are made, agents may need to be removed from or replaced in existing guidelines. Guidelines should avoid recommending use of nonformulary medications, and they can be useful in discouraging nonformulary medication use and guiding the appropriate use of nonformulary products when necessary.

Guidelines are frequently developed to address complex or particularly expensive medication therapies. However, complicated specialty therapies that will affect the care of very few patients may not justify the time and resources necessary to develop and maintain a guideline. Guidelines may be medication specific or disease oriented and may overlap in their scope of coverage.

The development of a clinical practice guideline should begin with the synthesis of all available biomedical evidence addressing the guideline topic. In many cases, guidelines from other organizations, both national and local, can be used as a starting point for development. The national guideline clearinghouse sponsored by the Agency for Healthcare Research and Quality is a useful source of previously developed guidelines ([www.guideline.gov](http://www.guideline.gov)). The subsequent consensus process, eliciting feedback and input from local stakeholders, is critical. Stakeholders may not reach unanimous agreement about all dimensions of the guideline, but their involvement in its development increases

their awareness of it and may create a sense of investment in its goals. Process-of-care and outcomes data from the organization's MUE activities (or, in some organizations, from such sources as the electronic medical records and computerized prescriber-order-entry systems) can also be used to make informed decisions during the consensus process. After the consensus process is completed, the guideline should be reviewed and approved by the P&T committee.

The dissemination and implementation of guidelines in the practice environment must also be carefully executed. Unlike active intervention tools that directly influence behavior, guidelines change behavior only when they are accessed, read, accepted, and put into practice. Exhaustive communication about the availability of guidelines is necessary. The dissemination of guidelines in hardcopy format is common, but electronic distribution (often in the form of a library of guidelines available via the Internet) is more efficient. Given the dynamic nature of the biomedical evidence and the quickening pace of changes in practice, maintaining current practice guidelines is an important challenge. Every guideline should include a time frame for future review and revision. If resources are not available to properly update and revise an older guideline, the guideline should be retired and removed from circulation.

**Off-Label Use.** The use of a drug prescribed for an indication not specifically approved by FDA is often referred to as off-label use. Off-label use can include the use of pharmaceuticals outside of specified populations, for different diseases or stages of diseases, or by different routes of administration. Other types of off-label use involve changes to dosing or dosing schedules or in chronology or sequence of use.

Before considering off-label use, supporting safety and efficacy evidence must be carefully evaluated and a risk-benefit determination made, especially when alternatives with FDA-approved labeling are available for the intended off-label use.<sup>42</sup> When considering or reviewing off-label use, the P&T committee should use an evidence-based process. The approach to evaluating evidence and benefit developed by the U.S. Preventive Services Task Force is an example.<sup>43,44</sup>

The following principles should guide the off-label use of medications:

1. Off-label pharmaceutical prescribing should be based on published evidence, and patient safety should be the primary consideration.
2. When the off-label use of an agent is expected to occur frequently, the P&T committee should establish protocols guiding that use. The P&T committee should be considered the arbiter of off-label use and should rely on the scientific evidence to guide its decisions.
3. The ultimate responsibility for the safety and efficacy of off-label use resides with the prescriber, who should be familiar with the evidence before considering off-label use, be aware of local protocols for use of the agent, and, when necessary, consult with an appropriately knowledgeable pharmacist.
4. Proper assessment of evidence for off-label use should involve as comprehensive and balanced a review as possible. Selective use of studies to support a position is strongly discouraged and, in the event of a negative

outcome, may not withstand the rigor of a thorough peer review.

**Research Pharmaceuticals (Investigational Drugs).** An investigational drug is defined as a chemical or biological used in a clinical investigation and can include prescription and nonprescription drugs, nutritional supplements, and herbal preparations. Investigational drug study procedures must be consistent with all applicable laws and regulations. Efforts should be made to ensure that the prescribing and distribution of investigational drugs benefit from the safe medication management systems used for other medications. More information on the management of investigational drugs can be found in other ASHP guidelines.<sup>45,46</sup>

**MUE Process.** Although distinctions have historically been made among the terms *drug-use evaluation*, *drug-use review*, and *medication-use evaluation*, they all refer to the systematic evaluation of medication use employing standard, observational quality-improvement methods (e.g., traditional “plan-do-check-act” approach). MUE is a quality-improvement activity, but it can also be considered a formulary system management technique.

MUE methods have traditionally involved establishing evidence-based criteria for medication use and applying those criteria retrospectively to determine the degree to which a particular medication was used in discordance with established criteria. Interventions could then be used to improve prescribing based on those data. As electronic medical records have become increasingly important and more widely available, MUE activities have matured from simple paper-based medical record reviews to sophisticated analyses drawing on multiple sources of data regarding medication use. A more expansive approach to MUE has been described in which not only the use of individual medications but the entire process of care for disease states is examined.<sup>47</sup> The use of quasiexperimental research methods may provide more meaningful information for quality-improvement purposes (e.g., economic, clinical, and humanistic outcomes of greater relevance than arbitrarily set appropriateness criteria).

MUE can be simply informative (collecting data to guide decision-making) or be used to measure the effect of interventions, such as the addition of a new agent to the formulary or the implementation of a new medication-use policy. MUE activities can focus on any dimension of the medication-use process (from medication acquisition to patient monitoring) that presents an opportunity for improvement. While MUE often focuses on problem-prone, high-risk, or high-cost medications, MUE can be used to examine any aspect of medication use that is problematic to the institution conducting the evaluation.

A systematic plan to monitor, evaluate, and improve medication use should be established within the organization.<sup>17</sup> Such a plan is an accreditation requirement for many organizations (e.g., Joint Commission<sup>26</sup>). MUE should be a part of the organization’s overall quality-improvement program. MUE activities should be conducted to examine the effect of medication-use policy decisions (particularly those made in the absence of convincing evidence from the biomedical literature) but can also be conducted to inform decision-making (again, particularly when making policy decisions under conditions of uncertainty). Specific projects to evaluate medication use can either involve assessing

how an individual medication is used or evaluate medication management of a given disease state. All steps of the medication-use process should be evaluated over time. The P&T committee, or its equivalent, should be involved in the MUE process.

Concurrent evaluation (collecting data during care delivery and sometimes as a component of the care process) is usually preferred over retrospective methods because it allows organizations to select relevant outcomes for collection rather than rely on outcomes routinely documented in patient medical records. For example, quality-of-life measures remain an infrequently documented measure in medical records. Only through concurrent evaluation can that outcome measure be reliably captured. Medications recently added to the formulary should be evaluated, especially if there is the potential for inappropriate use or adverse effects of concern. This review should occur 6–12 months after their addition to the formulary. High-cost, high-use, and problem-prone medications are also good candidates for evaluation.

### Incorporating Patient Safety Issues in the Decision-Making Process

P&T committees have always addressed medication safety issues. However, as medication errors have received increased scrutiny and more is understood about the process failures that contribute to such errors, P&T committees have more opportunities to address patient safety issues. The P&T committee should systematically address patient safety as part of its deliberations. Opportunities for including patient safety in P&T committee deliberations include the following:

1. When evaluating a medication for inclusion on the formulary, the P&T committee should consider adverse effects, issues in preparation, sound-alike or look-alike potential, and dosing or administration issues. Assessments should be conducted to identify potential safety concerns posed by use of the medication. The P&T committee should make recommendations for managing identified risks.
2. Organizations, in collaboration with the appropriate committees, should undertake projects to proactively assess risk in medication-use processes. The use of high-risk medications or major system changes (e.g., a new computer system, new equipment) offer opportunities to perform proactive risk assessments. Failure mode and effects analysis (FMEA) can be used to structure these assessments. The Joint Commission, Institute for Healthcare Improvement, and National Center on Patient Safety provide information about conducting and examples of FMEA projects on their websites ([www.jointcommission.org/](http://www.jointcommission.org/), [www.ihl.org/](http://www.ihl.org/), and [www.patientsafety.gov](http://www.patientsafety.gov)).
3. The P&T committee should consistently review medication-event data, including data on near misses, and make recommendations to prevent future events.
4. The P&T committee should conduct targeted quality-improvement projects to improve the safety of specific medications or to evaluate the processes involved.
5. When reviewing policies, the P&T committee should ensure that the policies adequately address the potential risk issues.

6. The P&T committee should champion evidence-based fail-safe techniques (e.g., bar-coding) to prevent medication events.
7. The P&T committee should review information available on patient safety or events reported by other organizations to identify ways to prevent medication events and disseminate the information to health care providers and, when appropriate, patients.

Resources on medication safety should be routinely reviewed to identify potential issues an organization could address. Examples of resources include the Institute for Safe Medication Practices ([www.ismp.org](http://www.ismp.org)), Medwatch ([www.fda.gov/medwatch](http://www.fda.gov/medwatch)), FDA Patient Safety News ([www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/)), and the U.S. Pharmacopeia Patient Safety Program ([www.usp.org/hqi/patientSafety/](http://www.usp.org/hqi/patientSafety/)).

## Drug Product Shortages

Health systems frequently need to address drug product shortages. Drug product shortages disrupt patient care and the processing of medication orders, increasing the risks presented by all aspects of the medication-use system, including purchasing, storage, pharmacy computer and automation systems, ordering, preparation, administration, and monitoring.

During a drug product shortage, the P&T committee plays an important role in setting organizational priorities. The P&T committee needs to develop strategies to address shortages in a timely manner, including designating appropriate alternatives, identifying strategies for rationing available drug product, establishing use restrictions, and implementing evidence-based review procedures. Therapeutic interchange can be useful in dealing with critical drug product shortages. When necessary, the P&T committee should work collaboratively with other committees and departments, such as risk management or specific medical departments affected by the shortage, to develop effective management plans for addressing shortages. Many organizations include a drug shortage update as a regular agenda item for the P&T committee. Communication with patients and staff is crucial to effectively manage shortages.

More information about managing drug product shortages can be found in the ASHP Guidelines on Managing Drug Product Shortages.<sup>48</sup>

## Implementing Medication-Use Policies

Various tools can be used to implement medication-use policies. The policy should be integrated directly into the therapeutic decision-making processes that guide the use of a medication as the health care professional orders it or incorporated into a preprinted order form. Other specific ways of communicating information about a medication-use policy may include the use of

- Inservice education,
- Grand rounds,
- Interactions between pharmacists and prescribers at the time of prescribing or dispensing,
- Staff meetings,
- e-mail,

- Newsletters,
- Mailings,
- Prescriber detailing, and
- Pharmacy or institutional websites.

Pilot or demonstration projects may be beneficial in illustrating the value of a new medication-use policy and may generate data that could justify a decision or help communicate why a specific policy is necessary.

## Conclusion

A formulary system is the multidisciplinary, evidence-based process employed by an organization to select and use medications that offer the best therapeutic outcomes while minimizing potential risks and costs for patients. Organizations employ the MUE process to continually improve how medications are used within the organization at all steps in the medication-use process. Medication use is an inherently complex and dangerous process that requires constant evaluation. Organizations need to implement tools and processes necessary to meet the goals of using medications effectively and safely. Professionals involved in the medication-use process need to know and understand how the organization's medication-use policies and processes can be incorporated into their daily work so that medications are used appropriately and safely. Technology offers many opportunities to make those processes more effective. Communicating the actions related to medication use is a constant challenge that organizations need to address.

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## Appendix—Glossary of Terms

**Formulary:** A continually updated list of medications and related information, representing the clinical judgment of physicians, pharmacists, and other experts in the diagnosis, prophylaxis, or treatment of disease and promotion of health.

**Formulary System:** An ongoing process whereby a health care organization, through its physicians, pharmacists, and other health care professionals, establishes policies on the use of drug products and therapies and identifies drug products and therapies that are the most medically appropriate and cost-effective to best serve the health interests of a given patient population.<sup>1</sup>

**Generic Substitution:** The substitution of drug products that contain the same active ingredient or ingredients and are chemically identical in strength, concentration, dosage form, and route of administration to the drug product prescribed.<sup>1</sup>

**Medication:** Any prescription medications, herbal remedies, vitamins, nutraceuticals, nonprescription drugs, vaccines, or diagnostic and contrast agents used to diagnose, treat, or prevent disease and other abnormal conditions and radioactive medications, respiratory therapy treatments, parenteral nutrition, blood derivatives, intravenous solu-

tions (plain or with electrolytes or drugs), or any product designated by the Food and Drug Administration as a drug (including investigational drugs).<sup>26</sup>

**Medication-Use Evaluation:** A performance-improvement method that focuses on evaluating and improving medication-use processes with the goal of optimal patient outcomes.<sup>17</sup>

**Pharmacy and Therapeutics (P&T) Committee:** An advisory committee that is responsible for developing, managing, updating, and administering a formulary system.<sup>1</sup>

**Therapeutic Alternatives:** Drug products with different chemical structures but of the same pharmacologic or therapeutic class and usually have similar therapeutic effects and adverse-reaction profiles when administered to patients in therapeutically equivalent doses.<sup>1</sup>

**Therapeutic Interchange:** Authorized exchange of therapeutic alternatives in accordance with previously established and approved written guidelines or protocols within a formulary system.<sup>1, 41</sup>

**Therapeutic Substitution:** The act of dispensing a therapeutic alternative for the drug product prescribed without prior authorization of the prescriber. This is an illegal act because only the prescriber may authorize an exchange of therapeutic alternatives.<sup>1</sup>

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Approved by the ASHP Board of Directors on January 28, 2008. These guidelines supersede the ASHP Guidelines on Formulary System Management dated November 20, 1991, the ASHP Technical Assistance Bulletin on Drug Formularies dated November 14, 1990, and the ASHP Technical Assistance Bulletin on the Evaluation of Drugs for Formularies dated November 19, 1987. Developed through the ASHP Council on Pharmacy Practice.

ASHP gratefully acknowledges the expert panel that developed these guidelines: Linda S. Tyler, Pharm.D., FASHP; Mirta Millares, Pharm.D., FCSHP, FASHP; Andrew L. Wilson, Pharm.D., FASHP; Lee C. Vermeulen, Jr., B.S.Pharm., M.S.; J. Russell (Rusty) May, Pharm.D., FASHP; Michael A. Valentino, R.Ph. MHSA; and Sabrina W. Cole, Pharm.D.

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The bibliographic citation for this document is as follows: American Society of Health-System Pharmacists. ASHP guidelines on the pharmacy and therapeutics committee and the formulary system. *Am J Health-Syst Pharm.* 2008; 65:1272–83.