

House of Delegates

Board of Directors Report: Policy Recommendations for the November 2019 Virtual House of Delegates

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COUNCIL ON THERAPEUTICS

POLICY RECOMMENDATIONS

The Council on Therapeutics is concerned with ASHP professional policies related to medication therapy. Within the Council's purview are (1) the benefits and risks of drug products, (2) evidence-based use of medicines, (3) the application of drug information in practice, and (4) related matters.

Nish Kasbekar, Board Liaison

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1. Research on Drug Use in Obese Patients

- 1 To encourage drug product manufacturers to conduct and publish pharmacokinetic and
- 2 pharmacodynamic research in obese patients to facilitate safe and effective dosing of
- 3 medications in this patient population, especially for medications most likely to be
- 4 affected by obesity; further,

- 5 To encourage manufacturers to include in the Food and Drug Administration (FDA)–
- 6 approved labeling detailed information on characteristics of individuals enrolled in drug
- 7 dosing studies; further,

- 8 To advocate that the FDA develop guidance for the design and reporting of studies that
- 9 support dosing recommendations in obese patients; further,

- 10 To advocate for increased enrollment and outcomes reporting of obese patients in
- 11 clinical trials of medications; further,

- 12 To encourage independent research on the clinical significance of obesity on drug use, as
- 13 well as the reporting and dissemination of this information via published literature,
- 14 patient registries, and other mechanisms; further,

- 15 To recognize that pharmacists are medication therapy experts who should provide
16 guidance on appropriate drug dosing for obese patients.

(Note: This policy would supersede ASHP policy 1515.)

Rationale

Given the growing rate of obesity in the United States, ASHP is concerned about the uncertainty surrounding how obesity affects drug dosing, effectiveness, and safety, especially for medications most likely to be affected by obesity (defined as body mass index of $>30 \text{ kg/m}^2$). The FDA does not require that studies of obese patient populations be performed, despite the growing proportion of obese patients in United States. Obese patients are subject to variable pharmacokinetic effects of oral, parenteral, and topical therapeutic agents.

Drug product manufacturers should be encouraged to complete pharmacokinetic and pharmacodynamic dosing studies of obese patients, especially for drugs for which obesity is expected to have a significant clinical impact (e.g., antimicrobials, highly lipophilic drugs). If these voluntary studies are not completed, then manufacturers should include in the FDA-approved labeling complete information on the population enrolled in dosing studies and the methods used to determine dosing so that clinicians can assess the extent to which that population reflects patients being treated.

ASHP advocates that the FDA develop guidance for voluntary drug dosing studies of obese patients that would define study design and reporting with the intent of standardizing this research to the extent possible. The need for this guidance is supported by the complexity of drug dosing for obese patients, which varies based on drug and patient characteristics. A paucity of research in this population is noted, similar to the lack of preapproval studies in geriatric and pediatric patients. Such studies could help standardize research methods and promote comparative effectiveness research. ASHP also encourages independent clinical and practice-based research to further define clinical use of drugs in the treatment of obese patients, as well as clinician reporting of patient experience in articles and clinical registries.

ASHP also believes that pharmacists are uniquely positioned to review and apply this literature to make dosing recommendations based the most appropriate weight classification for obese patients, including ideal body weight, adjusted body weight, or total body weight.

Background

The Council reviewed ASHP policy 1515, Research on Drug Use in Obese Patients, as part of sunset review. The Council voted to recommend revising 1515 to read as follows (underscore indicates new text):

To encourage drug product manufacturers to conduct and publish pharmacokinetic and pharmacodynamic research in obese patients to facilitate safe and effective dosing of medications in this patient population, especially for medications most likely to be affected by obesity; further,

To encourage manufacturers to include in the Food and Drug Administration (FDA) – approved labeling detailed information on characteristics of individuals enrolled in drug dosing studies; further,

To advocate that the FDA develop guidance for the design and reporting of studies that support dosing recommendations in obese patients; further,

To advocate for increased enrollment and outcomes reporting of obese patients in clinical trials of medications; further,

To encourage independent research on the clinical significance of obesity on drug use, as well as the reporting and dissemination of this information via published literature, patient registries, and other mechanisms; further,

To recognize that pharmacists are medication therapy experts who should provide guidance on appropriate drug dosing for obese patients.

The Council noted that the policy is still required but was in need of updating, particularly regarding the need for pharmacist expertise.

2. Testing and Documentation of Penicillin Allergy as a Component of Antimicrobial Stewardship

- 1 To advocate involvement of pharmacists in the clarification and assessment of penicillin
- 2 allergy, intolerance, and adverse drug events; further,

- 3 To advocate for documentation and de-labeling of penicillin allergies, intolerances,
- 4 reactions, and severities in the medical record when appropriate to facilitate optimal
- 5 antimicrobial selection; further,

- 6 To recommend the use of penicillin skin testing, graded antibiotic challenges, and oral
- 7 direct challenges in appropriate candidates when clinically indicated to optimize
- 8 antimicrobial selection; further,

- 9 To support the education and training of pharmacists in the assessment, management,
- 10 and documentation of penicillin allergies, intolerances, and adverse events; further,

- 11 To advocate that state board of pharmacy regulations include penicillin allergy skin
- 12 testing under pharmacists' scope of practice.

(Note: This policy would supersede ASHP policy 1517.)

Rationale

Approximately 10% of all patients in the United States report having a penicillin allergy; however, only 1 in 10 patients with a labeled penicillin allergy are truly allergic. Furthermore, approximately 80% of patients with an IgE-mediated penicillin allergy lose their sensitivity after 10 years. Specific rates of cross-reactivity between penicillins and cephalosporins vary depending on specific resources, although the likelihood of cross-reactivity is lower than previously described. Historically, it has been estimated that 10% of patients with a true penicillin allergy will experience an allergic reaction if administered a cephalosporin, but this data is from early cross-reactivity studies with potential contamination of early cephalosporin products with penicillin G. More recent data suggest cross-reactivity rates of less than 1%. Cross-reactivity is more closely associated with structurally similar R-1 side chains than with the beta-lactam ring itself.

Penicillin allergies have led to considerable public health risks and unintended consequences, including receipt of more broad-spectrum antibiotics, suboptimal therapy for infectious disease management, more antibiotic-related costs, increased risk of adverse effects, and increased risk of methicillin-resistant *Staphylococcus aureus* and *Clostridioides difficile*. As such, structured and thorough interview assessments with appropriate documentation and de-labeling of penicillin allergies are necessary to combat these potential negative consequences of labeled penicillin allergies. Penicillin skin testing and graded or oral challenges are excellent opportunities to assist in the assessment and de-labeling of penicillin allergies. Although pharmacists are well positioned to be involved in these processes, state boards of pharmacy have different regulations regarding whether penicillin skin testing is within pharmacists' scope of practice. Penicillin allergy assessment, management, and documentation are excellent opportunities to improve pharmacist involvement in patient care and to improve antimicrobial stewardship initiatives for health systems, and offer a potential opportunity for pharmacists to bill for their services.

The American Academy of Allergy, Asthma, and Immunology, as part of the [Choosing Wisely](#) campaign, recommends against the overuse of non-beta-lactam antibiotics in patients with a history of penicillin allergy, without appropriate evaluation. In a research abstract from the Canadian Society of Allergy and Clinical Immunology meeting in 2014, researchers found that only 15% of hospital-discharged patients notified a family physician of a negative penicillin allergy evaluation; at the same time, 30% were still listed as penicillin allergic upon readmission to the hospital. Additionally, the existence of a pharmacist-provided allergy skin test has proven to positively impact patient care by optimizing antibiotic regimens and accelerate discharges for patients while reducing healthcare costs.

Background

The Council discussed ASHP policy 1517 as part of sunset review. The Council voted to recommend revising 1517 to read as follows (underscore indicates new text; ~~strikethrough~~ indicates deleted text):

To advocate involvement of pharmacists in the clarification and assessment of penicillin

allergy, intolerance, and adverse drug events; further,

To advocate for documentation and de-labeling of penicillin allergies, intolerances, reactions, and severity ies in the medical record when appropriate to facilitate optimal antimicrobial selection; further,

To recommend the use of penicillin skin testing, graded antibiotic challenges, and oral direct challenges in appropriate candidates when clinically indicated to optimize antimicrobial selection; further,

To support the education and training of pharmacists in the assessment, management, and documentation of penicillin allergies, intolerances, and adverse events; further,

To advocate that state board of pharmacy regulations include penicillin allergy skin testing under pharmacists' scope of practice.

The Council also recommended changing the title of the policy to “Testing and Documentation of Penicillin Allergy as a Component of Antimicrobial Stewardship” to reflect the updates to the policy language and rationale.

3. Antimicrobial Use in Agriculture

1 To advocate that the Food and Drug Administration (FDA) eliminate future approval of
2 antimicrobials for nontherapeutic uses in agricultural animals that represent a safety
3 risk by contributing to antimicrobial resistance; further,

4 To encourage efforts to phase out and eliminate the nontherapeutic uses of
5 antimicrobials previously approved by the FDA; further,

6 To support the therapeutic use of antimicrobials in animals only under the supervision
7 of a veterinarian; further,

8 To encourage the agricultural industry to report to the appropriate regulatory bodies
9 the specific antimicrobials used, the purpose or indication for their use, and the settings
10 in which they are used; further,

11 To encourage the FDA, Centers for Disease Control and Prevention, and other
12 stakeholders to monitor and limit, when effective alternatives are available, the
13 therapeutic use of antimicrobials that are essential to the treatment of critically ill
14 human patients; further,

15 To advocate for the inclusion of pharmacists in antimicrobial surveillance and related

- 16 public health efforts based on pharmacists' knowledge of antimicrobial drug products
17 and antimicrobial resistance.

(Note: This policy would supersede ASHP policy 1009.)

Rationale

The use of antibiotics in animal agriculture represents the majority of antibiotic use worldwide and poses significant public health risks. Approximately 80% of antibiotic consumption in the U.S. is dedicated to agricultural purposes. Despite warnings and risks, antibiotics are still excessively used for growth promotion, feed efficiency, and disease prevention in animal agriculture.

ASHP supports the public health approach to antimicrobial use in agricultural animals outlined in the July 2010 FDA [testimony](#) to Congress. The goal of this approach is to minimize the development of antimicrobial resistance, preserving the effectiveness of antimicrobial therapies that are critical in human medicine. According to the FDA, an enhanced action plan would seek to phase out the use of antimicrobials for nontherapeutic purposes (e.g., animal growth promotion, food efficiency) by eliminating future approvals for new nontherapeutic indications. ASHP also supports the FDA's request for increased statutory authority that would facilitate removal of previously approved nontherapeutic uses of antimicrobials. This two-pronged approach is critical to preserving the effectiveness of existing antimicrobials as well as those in development. ASHP opposes nontherapeutic uses but supports animal use of antimicrobials for therapeutic purposes (e.g., treatment of disease or prevention of disease in animals within a population that has documented disease) when this use occurs under the supervision of a veterinarian. Reporting of the specific antimicrobials used, the purpose or indication for their use, and the settings in which they are used would support achievement of the FDA's action plan. In addition, ASHP advocates that FDA approval and subsequent use of antimicrobials should take into consideration the public health impact of the drugs' use. Pharmacists' knowledge of antimicrobial drugs and antimicrobial resistance will be critical to these efforts, including the identification of antimicrobial classes for which animal treatment use should be minimized in order to retain the effectiveness of these drugs for the treatment of critically ill human patients.

Background

The Council discussed ASHP policy 1009, Preservation of Antimicrobials for Medical Treatment, as part of sunset review. The Council voted to recommend revising policy 1009 to read as follows (underline indicates new text; ~~strikethrough~~ indicates deleted text):

To advocate that the Food and Drug Administration (FDA) eliminate future approval of antimicrobials for nontherapeutic uses in agricultural animals that represent a safety risk by contributing to ~~antibiotic~~ antimicrobial resistance; further,

To encourage efforts to phase out and eliminate the nontherapeutic uses of

antimicrobials previously approved by the FDA; further,

To support the therapeutic use of antimicrobials in animals only under the supervision of a veterinarian; further,

To encourage the agricultural industry to report to the appropriate regulatory bodies the specific antimicrobials used, the purpose or indication for their use, and the settings in which they are used; further,

To encourage the FDA, Centers for Disease Control and Prevention, and other stakeholders to monitor and limit, when effective alternatives are available, the therapeutic use of antimicrobials that are essential to the treatment of critically ill human patients; further,

To advocate for the inclusion of pharmacists in antimicrobial surveillance and related public health efforts based on pharmacists' knowledge of antimicrobial drug products and antimicrobial resistance.

The Council also recommended changing the title of the policy to "Antimicrobial Use in Agriculture" to reflect the updates to the policy language and rationale.

4. Appropriate Use of Testosterone

- 1 To discontinue ASHP policy 1536, Appropriate Use of Testosterone, which reads:
 - 2 To educate pharmacists, patients, and the public about the risks and benefits of
 - 3 testosterone use and about best practices for safe handling of testosterone,
 - 4 specifically regarding harmful effects of contact with another person; further,
 - 5 To educate healthcare providers about the importance of including accurate
 - 6 testosterone levels and confirmed evidence of clinical symptoms in the evaluation of
 - 7 candidates for testosterone therapy; further,
 - 8 To encourage additional research on the long-term effects of testosterone therapy.

Background

The Council discussed ASHP policy 1536 as part of sunset review. The Council recommended discontinuing the policy because there has been a significant decrease in the use of testosterone as data has demonstrated such use has led to more adverse effects than benefits. This change in practice has reduced inappropriate prescribing and its associated concerns.