

## Research

### **Drug Dosing in Conditions that Modify Pharmacokinetics or Pharmacodynamics (1804)**

*Source: Council on Therapeutics*

To encourage research on the pharmacokinetics and pharmacodynamics of drugs in acute and chronic conditions; further,

To advocate healthcare provider education and training that facilitate optimal patient-specific dosing in populations of patients with altered pharmacokinetics and pharmacodynamics; further,

To support development and use of standardized models, laboratory assessment, genomic testing, utilization biomarkers, and electronic health record documentation of pharmacokinetic and pharmacodynamic changes in acute and chronic conditions; further,

To collaborate with stakeholders in enhancing aggregation and publication of and access to data on the effects of such pharmacokinetic and pharmacodynamic changes on drug dosing within these patient populations.

*This policy supersedes ASHP policy 1720.*

### **Clinical Investigations of Drugs Used in Elderly and Pediatric Patients (1723)**

*Source: Council on Therapeutics*

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

To encourage drug product manufacturers to conduct pharmacokinetic and pharmacodynamic research in pediatric and geriatric patients to facilitate safe and effective dosing of medications in these patient populations.

*This policy supersedes ASHP policy 0229.*

### **Research on Drug Use in Obese Patients (1515)**

*Source: Council on Therapeutics*

To encourage drug product manufacturers to conduct 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 de-

tailed 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.

*This policy supersedes ASHP policy 1013.*

### **Institutional Review Boards and Investigational Use of Drugs (0711)**

*Source: Council on Pharmacy Practice*

To support mandatory education and training on human subject protections and research bioethics for members of institutional review boards (IRBs), principal investigators, and all others involved in clinical research; further,

To advocate that principal investigators discuss their proposed clinical drug research with representatives of the pharmacy department before submitting a proposal to the IRB; further,

To advocate that IRBs include pharmacists as voting members; further,

To advocate that IRBs inform pharmacy of all approved clinical research involving drugs within the hospital or health system; further,

To advocate that pharmacists act as liaisons between IRBs and pharmacy and therapeutics committees in the management and conduct of clinical drug research studies; further,

To strongly support pharmacists' management of the control and distribution of drug products used in clinical research.

*This policy was reviewed in 2016 by the Council on Therapeutics and by the Board of Directors and was found to still be appropriate.*

## ASHP Policy Positions 2009–2019 (with Rationales): Research

**1804**

### **Drug Dosing in Conditions that Modify Pharmacokinetics or Pharmacodynamics**

*Source: Council on Therapeutics*

To encourage research on the pharmacokinetics and pharmacodynamics of drugs in acute and chronic conditions; further,

To advocate healthcare provider education and training that facilitate optimal patient-specific dosing in populations of patients with altered pharmacokinetics and pharmacodynamics; further,

To support development and use of standardized models, laboratory assessment, genomic testing, utilization biomarkers, and electronic health record documentation of pharmacokinetic and pharmacodynamic changes in acute and chronic conditions; further,

To collaborate with stakeholders in enhancing aggregation and publication of and access to data on the effects of such pharmacokinetic and pharmacodynamic changes on drug dosing within these patient populations.

*This policy supersedes ASHP policy 1720.*

### **Rationale**

The pharmacokinetic and pharmacodynamic properties of drugs found in drug information monographs are based on the drug's absorption, distribution, metabolism, and excretion in healthy, adult patients during Phase I of a drug's clinical trials. Many patients receiving drug therapy do not fit this profile, and many have compromised organ function. The medical community has long recognized the need for a standardized approach to evaluating organ system dysfunction. Although there are methods to determine organ function (e.g., the Cockcroft-Gault equation for renal function or the Child-Turcotte-Pugh Classification for Severity of Cirrhosis), there is debate as to whether these methods are true indicators of organ function, as the components that comprise these equations may fluctuate based on severity and patient status. Traditional laboratory values used to evaluate organ dysfunction can be bidirectional and conflicting as well.

In addition, with the exception of adjustments for renal dysfunction, there is not much information regarding dosage adjustment for specific drugs. Many organ systems are involved in a drug's absorption, distribution, metabolism, and excretion. Hepatic effects, for example, are a risk area, as those effects are slower to be seen and have not been the subject of much research, and the number of drugs affected are smaller in number than renally excreted drugs. Both acute and chronic aspects of patient conditions may require monitoring and adjustment, including sepsis, encephalopathies, pregnancy, heart failure exacerbations, and cystic fibrosis. Certain protocols, such as therapeutic hypothermia, can also have clinically significant impact

on a drug's pharmacokinetic and pharmacodynamic behavior. There is also need to promote research and utilization of biomarkers into practice, as these may reflect organ function and may provide pharmacists with a more complete clinical picture.

Given the complex dose adjustments and variety of conditions, education of pharmacists and other healthcare professionals is critically important to appropriately treat patients.

### **1723**

#### **Clinical Investigations of Drugs Used in Elderly and Pediatric Patients**

*Source: Council on Therapeutics*

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

To encourage drug product manufacturers to conduct pharmacokinetic and pharmacodynamic research in pediatric and geriatric patients to facilitate safe and effective dosing of medications in these patient populations.

*This policy supersedes ASHP policy 0229.*

#### **Rationale**

Pediatric and geriatric patients are populations in which the pharmacokinetic and pharmacodynamic properties of medications may differ from those typically seen in an adult patient. These differences can dramatically alter the behavior of drugs, producing supra- or subtherapeutic levels, which may result in adverse effects. While there has been legislation that provides incentive for drug manufacturers to study these effects, many drugs already approved by the FDA do not have such information or robust outcomes reporting for these at-risk populations. The need for this guidance is supported by the complexity of drug dosing for these patients, which varies based on drug and patient characteristics. A paucity of research in these patient populations is noted, which is similar to the lack of preapproval studies in obese patients. ASHP also encourages independent clinical and practice-based research to further define clinical use of drugs in the treatment of these patients, as well as clinician reporting of patient experience via published articles and clinical registries.

### **1515**

#### **RESEARCH ON DRUG USE IN OBESE PATIENTS**

*Source: Council on Therapeutics*

To encourage drug product manufacturers to conduct 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.

*This policy supersedes ASHP policy 1013.*

**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. The FDA does not require that studies of obese patient populations be performed, despite the growing proportion of obese patients in America. Obese patients are subject to variable pharmacokinetic effects of oral and injectable 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 significant clinical impact (e.g., antimicrobials, highly lipophilic drugs, etc.). 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.