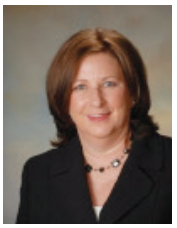
Inactive Ingredients and Drug Therapy Safety



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THE GOLD STANDARD OF QUALITY PHARMACY

practice has been the assurance that the correct drug is prescribed and dispensed for optimal patient clinical outcomes and safety. Assuming the drug prescribed is correct for the patient and indication, the pharmacy system provides the pharmacist with multiple avenues to assure the drug is accurately dispensed and evaluated for clinical appropriateness and safety. Features include data-driven technology to identify the correct product for substitution, both chemically and legally. Clinical decision support parameters include allergy alerts, adverse events, drug-drug interactions, and therapeutic duplication warnings. System quality measures are primarily, but not exclusively, based on the drug's active ingredient(s). An increasing demand now exists to assess the safety of inactive ingredients. This becomes even more critical with the increase in polypharmacy and its associated risks, especially in the elderly and the immunocompromised populations.

WHY THE FOCUS ON INACTIVE INGREDIENTS?

In the past decade the United States has identified a documented increase in chemical allergies and intolerances. Peanut allergies have increased by 21% since 2010, with 2.5% of children in the United States with a reported peanut allergy. In the U.S. population, up to 1% (3.5 million people) have documented celiac disease, which is a fourfold increase from the 1950s. An additional 5% to 7% may be gluten intolerant. Lactose intolerance occurs in 65% of the human population after infancy, and has a much higher incidence in Hispanic and African-American populations. Allergies and intolerance conditions can result in a spectrum of reactions, from anaphylatic shock for a severe peanut allergy to mild gastric upset for a primary lactose intolerance.

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INACTIVE INGREDIENTS DEFINED

The FDA (Food and Drug Administration) defines inactive ingredient(s) as any component of a drug product other than the active ingredient. At times, a chemical entity could be defined as an active and an inactive ingredient. Alcohol is frequently present as an inactive ingredient but is also a drug active ingredient by itself. Peanut products and derivatives, lactose, and gluten derivatives are common inactive ingredients in drugs. Among common inactive ingredients, 38 are known allergens, including dyes and peanut oils. *The Harvard Health Letter* of July 2019 published a number of statistics around inactive ingredients. According to the *Health Letter*, 75% of tablets and capsules are composed of inactive ingredients and contain an average of nine inactive ingredients, and 93% contain one potential allergen.

Reporting thresholds become critical to differentiate the alert functions. Primary lactose intolerance would not need an alert for the quantity reported in most tablets; however, for secondary or congenital lactose intolerance, an alert could be critical. Peanut products would need a critical allergy alert regardless of the inactive ingredient quantity.

TECHNOLOGY DOWN IN THE WEEDS

The FDA has now provided new and improved tools to address the safety surrounding inactive ingredients. On July 29, 2020, the FDA announced significant

enhancements to the Inactive Ingredient Database. The FDA has initiated the reporting of the maximum daily exposure (MDE) information for prescription drug excipents. This data provides the ability to calculate the additive MDEs for patients on multiple drugs and provides the foundational data to support differential clinical reporting for allergies and intolerances across various medical conditions. In addition, the FDA has expanded search capabilities and committed to quarterly updates viewable via the Quarterly Inactive Ingredient Database Change Log. The database also has a download feature. A simple search for lactose identified over 10,000 drug products that contain lactose in varying amounts.

PHARMACY SYSTEM CHALLENGES

Challenges exist to execute the interoperability needed to access the FDA inactive ingredient data, codify and organize it into pharmacy system language, establish relationships between drug products and patient data, and develop a meaningful alert for the pharmacist. Manufacturers need to be compliant and timely with reporting changes of inactive ingredients to the FDA, in particular allergenic ingredients. The FDA should consider more frequent updates instead of quarterly. The FDA needs to establish standard criteria for gluten and gluten derivatives for inactive ingredient listing. The drug compendia should provide complete, accurate, and timely inactive ingredient data in a meaningful format, along with the accompanying MDE information usable for pharmacy systems.

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Pharmacy system developers will need to expand clinical alerting and decision support tools to manage the increasing amount of variance in doses and calculations around exposure of multiple inactive ingredients, as well as alert settings around allergies and tolerances depending on the patient's condition. As always, alert fatigue must be managed for clinicians. System developers will need to be aware that the use of representative NDCs (National Drug Codes) will not be feasible for inactive ingredients. Pharmacy systems often use representative NDCs for various functions; however, inactive ingredients differ from NDC to NDC. Accurate alerts and calculations would be dependent on the actual NDC dispensed.

Pharmacists and pharmacy systems will be the front-line defense for patients with these conditions. Pharmacists must acquire more accurate patient allergy and intolerances and keep them current. Pharmacists should be integral in the development of the pharmacy system tools to define, calculate, and report on inactive ingredient alerts and warnings. Patient safety documents will need to be examined and modified, as necessary.

IN SUMMARY

The ability of a pharmacy system to provide clinical management for patients with allergies and intolerances to "inactive ingredients" is critical to safety and should be considered a fundamental quality practice. How does your pharmacy system address inactive ingredients contained in prescription products? Does your patient profile allow for the entry of allergy information for common allergens found as inactive ingredients in drugs, including common chemical intolerances? **CT**

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