Transition to Albuterol HFA: *Are All Inhalers Interchangeable?*

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ABSTRACT

The prevalence of asthma in the United States is on the rise, and current asthma guidelines recommend prescribing short-acting beta agonists (albuterol) for treatment of reversible airway disease. Government regulations have imposed the transition from albuterol CFC (chlorofluorocarbon) to albuterol HFA (hydrofluroalkane). Prescribers must consider differences between CFC versus HFA inhalers, as well as variations among the available forms of albuterol HFA. Device design, increased cost for branded medication, patient preference, and a host of variables must be considered when deciding among the types of albuterol HFA for a given patient. Pharmacists and clinicians must partner together and recognize that all forms of albuterol are not interchangeable and thus improve asthma management.

Keywords: albuterol, beta agonist, chlorofluorocarbon, hydrofluroalkane

Starting January 1, 2009, albuterol inhalers containing chlorofluorocarbons (CFC) were discontinued in the United States. CFCs have been replaced by hydrofluroalkane (HFA), a more environmentally friendly propellant. This phase-out resulted from U.S. participation in an international treaty called the Montreal Protocol on Substances that Deplete the Ozone Layer.[1]

The prevalence of asthma is increasing and approximately 20 million Americans have been diagnosed with asthma.[2] National guidelines recommend all asthmatics have a short-acting beta agonist available for quick symptom relief and prevention of exercise-induced asthma. Chronic asthma management requires regular assessment of a patient's severity (mild intermittent, mild moderate, or severe persistent) and control (well, not well, or poorly controlled). The frequency of albuterol usage is both a marker of control and a measure of impairment due to disease severity.[3] As we transitioned

our patients to albuterol HFA, many questions arose that promoted discussion and inquiry into the similarities and differences of the current rescue inhalers. These considerations may help to guide clinicians' choices and how pharmacists fill the prescriptions for such inhalers.

In the United States, the available forms of albuterol HFA are ProAir HFA, Proventil HFA, and Ventolin HFA. Other options for treatment and prevention of bronchospasm in reversible airway disease include levalbuterol HFA (Xopenex) and pirbuterol acetate (MaxAir Autohaler, a breath-actuated device that still contains CFC). All HFA products underwent clinical development and completed new drug applications through the FDA. Thus, no generic formulations are or will be available until current patents expire.[1]

EQUIVALENCE OF ALBUTEROL HFA AND ALBUTEROL CFC

To investigate pharmacy dispensing patterns regarding albuterol HFA, we polled 58 local pharmacists; 35 (60%) responded. Interestingly, most pharmacists believed all forms of albuterol are equivalent and thus interchangeable. Likewise, in the opinion of most pharmacists, ProAir was generally considered a generic alternative. In fact, the FDA has deemed that *the formulations are not biologically equivalent*.[4] Therefore, by law, pharmacists cannot substitute an albuterol formulation even if signed as *Substitution Allowed* unless they check with the prescribing provider. Finally, when asked if pharmacists notified prescribers when patients filled albuterol too often, all responded that they did. When prompted to define "too often," answers were widely inconsistent, highlighting that pharmacists vary in their definition and threshold of overuse.

While we did not poll prescribers, our survey confirmed the need for further education among all health care providers in adjusting the switch to albuterol HFA. The limited survey raised questions regarding basic knowledge of asthma guidelines, which indicate lack of asthma control if patients use albuterol greater than twice a week (albuterol used as exercise prophylaxis not counted) or require greater than 2 albuterol canisters (200 actuations per canister) per year.[3]

DEVICE CONSIDERATIONS

When compared to albuterol CFC, albuterol HFA has a slightly different smell and taste and the spray is reported to be less forceful and warmer.[5] Each formulation may or may not have excipients (an inactive ingredient used as a carrier for the active drug). As well, they have different valve systems, both in material and in shape (Table 1). Subsequently, each HFA inhaler has its own unique plume to its spray and aerodynamic flow characteristics, influencing patient acceptance and potential for lung deposition. Lastly, optimal (open mouth vs closed mouth) technique and the need for and utility of spacer devices with HFA inhalers has not been adequately explored or defined.

Unlike CFC inhalers, HFA inhalers require frequent priming and cleaning of these devices to ensure proper drug delivery.[1] All inhalers should be primed by releasing up to 4 test sprays before the first dose and again if the device has not been used for 2 weeks.[6-8] While each inhaler has specific directions for the individual device, it is generally recommended to wash the plastic mouthpiece weekly in warm water for 30 seconds and then air dry thoroughly. Patient compliance is likely to be low in this regard.

Clogging of HFA inhalers has been reported and may be associated with insufficient device cleaning. Thirty-two of each type of inhaler (Ventolin, ProAir, and Proventil) were actuated every 4 hours until the device clogged or dose limit was reached. More than half of the unwashed Proventil inhalers clogged, while none of the properly washed devices clogged.[9]

COST CONSIDERATIONS

An important consideration for prescribers of albuterol HFA is the increased cost of branded albuterol HFA versus the previously available generic albuterol CFC. In our geographic area, we polled 7 retail and 1 local pharmacy regarding costs of ProAir HFA, Proventil HFA, and Ventolin HFA. While the price range among the 3 inhalers was relatively comparable, a wide range of prices exists with any given inhaler and the different dispensing pharmacies. More specifically, ProAir ranged from $35.99 to $58.97, Proventil from $42.79 to $54.09, and Ventolin from $34.50 to $53.97. These price ranges also reflect

Table 1. Device Differences

	Spacer	Valve Stem	Excipients
ProAir HFA	Round	Plastic	Ethanol
Proventil HFA	Oval	Aluminum	Ethanol and oleic acid
Ventolin HFA	Oval	Plastic	None