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## The Impact of CFC-to-HFA Conversion

### What Pharmacists Need to Know

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# The Impact of CFC-to-HFA Conversion

## What Pharmacists Need to Know

Marsha K. Millonig, R.Ph., MBA

In 1987, environmental concerns led to an international agreement called the Montreal Protocol on Substances that Deplete the Ozone Layer (Montreal Protocol) that provided for the phaseout of chlorofluorocarbons, or CFCs, which have been shown to damage the earth's protective ozone layer. Medical products that are considered essential, such as asthma inhalers, are temporarily exempt from the CFC ban but only until ozone-friendly alternatives become available. The Food & Drug Administration (FDA) issued a final regulation on March 31, 2005, that requires the phaseout of all CFC albuterol metered-dose inhalers by December 31, 2008. The transition from CFC to hydrofluoroalkane, or HFA, inhalers will require pharmacists to educate patients on changes in taste, spray characteristics,

and trailing effects among others. Keeping patients compliant with therapy is essential for cost-effective management of asthma and chronic obstructive pulmonary disease (COPD).

### The Montreal Protocol

During the 1970s, scientists became aware of a relationship between the level of stratospheric ozone and industrial use of CFCs. Ozone ( $O_3$ ), which causes respiratory problems when it occurs in elevated concentrations near the ground, shields the Earth from potentially harmful solar radiation when in the stratosphere.<sup>1</sup> Excessive exposure to solar radiation is associated with adverse health effects, such as skin cancer and cataracts, as well as other

## Learning Objectives

After completing this continuing education article, pharmacists should be able to:

- ▶ Describe how CFC (chlorofluorocarbon) use in aerosols became an environmental issue and list highlights of the Montreal Protocol;
- ▶ Summarize the FDA's phaseout process for CFC inhalers;
- ▶ Interpret the importance of the pharmacist as the primary source of information for patients related to the conversion of aerosols from CFC to HFA (hydrofluoroalkane) propellants;
- ▶ Discuss the prevalence of asthma and chronic obstructive pulmonary disorder (COPD), associated treatment guidelines, and the use of inhalers in their treatment;
- ▶ Explain how inhaler formulations change with the conversion from CFC- to HFA-based products, including taste and spray characteristics;
- ▶ Describe steps that need to be taken with patients when converting them from CFC- to HFA-based inhalers, including dosing considerations and cost implications; and
- ▶ Explain the pharmacist's role in getting information to patients on the conversion and steps that can be taken to do so.

adverse environmental effects. Emissions of CFCs and other ozone-depleting substances (ODSs) reduce stratospheric ozone concentrations through a catalytic reaction, thereby allowing more solar radiation to reach the Earth's surface. Because of this, environmental scientists from the United States and other countries advocated ending all uses of these chemicals.<sup>2</sup>

CFCs are organic compounds that contain carbon, chlorine, and fluorine atoms. CFCs were first used commercially in the early 1930s as a replacement for hazardous materials then used in refrigeration, such as sulfur dioxide and ammonia. Subsequently, CFCs were found to have a large number of uses, including as solvents and as propellants in self-pressurized aerosol products, such as metered-dose inhalers (MDIs). CFCs are very stable in the troposphere, the lowest part of the atmosphere. They move to the stratosphere, a region that begins about 6 to 10 miles above Earth's surface and extends up to about 31 miles altitude. Within the stratosphere, there is a zone about 10 to 25 miles above the Earth's surface in which ozone is relatively highly concentrated—the ozone layer. Once in the stratosphere, CFCs are gradually broken down by strong ultraviolet light, where they release chlorine atoms that then deplete ozone (Figure 1). Depleting ozone allows more ultraviolet-B (UV-B) radiation to reach the Earth's surface, where it increases skin cancers and cataracts, and damages some marine organisms, plants, and plastics.<sup>3</sup> In the late 1980s, scientists began searching for CFC replacements. The most suitable compounds identified were the hydrofluoroalkanes HFA 134a (tetrafluoroethane) and HFA 227 (heptafluoropropane), collectively known as HFAs.<sup>4</sup> The first CFC-free inhaler, salbutamol sulphate MDI, was launched in 1995 and marketed as Airomir™ or Epaq™ in Europe, New Zealand, and Asia, and as Proventil-HFA™ in the USA by 3M Pharmaceuticals.

The international effort to craft a coordinated response to the global environmental problem of stratospheric ozone depletion culminated in the Montreal Protocol, an international agreement to regulate and reduce production of ODSs. The United States became a party to the Montreal Protocol on Substances that Deplete the Ozone Layer (Montreal Protocol) on January 1, 1989. The Mon-

treau Protocol project's Web site may be accessed at <http://www.unep.org/ozone/pdfs/Montreal-Protocol2000.pdf>. The United States played a leading role in the negotiations of the Montreal Protocol, believing that internationally coordinated control of ozone-depleting substances would best protect both the U.S. and global public health and the environment from potential adverse effects of depletion of stratospheric ozone.

One hundred and eighty-six countries have now ratified the Montreal Protocol, and the overall usage of CFCs has been dramatically reduced. In 1986, global consumption of CFCs totaled about 1.1 million metric tons annually, and by 2000, total annual consumption had been reduced to fewer than 0.1 million metric tons.<sup>5</sup> This decline amounts to about a 90% decrease in consumption and is a key measure of the success of the Montreal Protocol. Within the United States, consumption of ODSs, and CFCs in particular, has fallen sharply—consumption of CFC-11 and CFC-12 is about 20% of 1990 consumption.

Under the Montreal Protocol, production of CFCs in any year by any country is banned after the phaseout date unless the Parties to the Montreal Protocol agree to designate the use as "essential" and approve a quantity of new production for that use. Each year, each Party nominates the amount of CFCs needed for each essential use and provides the reason why such use is essential. Agreement on both the essentiality and the amount of CFCs needed for each nominated use has been reached by consensus at the annual meeting of the Parties. EPA has generated a series of estimates of the environmental and public health benefits of the Montreal Protocol between 1990 and 2165 if the treaty is fully implemented.<sup>6</sup> The benefits include:

- reductions of nonfatal skin cancers by hundreds of millions;
- six million fewer fatalities due to skin cancer;
- 27.5 million cataracts avoided.

The value of these and related benefits is estimated to equal \$4.3 trillion in present value when discounted at 2% over the period of 175 years or about \$6 trillion after adjusting for inflation between 1990 and 2004. This estimate includes all benefits of total global ODS emission



Allergy Drugs Advisory Committee meeting in June 2004, as well as consultation with other Federal agencies, helped the agency develop the final rule.

The FDA final rule gives manufacturers significantly more time to make the transition to CFC-free products than some experts had recommended. In June 2004 members of the FDA's Pulmonary-Allergy Drugs Advisory Committee suggested that CFC-based albuterol products be phased out by Dec. 31, 2005. The FDA said the new phaseout date would give manufacturers of CFC-free inhalers enough time to ramp up production of their products to ensure there are enough environmentally friendly inhalers to meet public demand.

Some advisory committee members had expressed concerns that manufacturers would not have enough time to increase production of albuterol non-CFC inhalers by the end of 2005. Manufacturers had also expressed some reservations about the Dec. 31, 2005, date, including the two companies that at the time made CFC-free inhalers, GlaxoSmithKline, which makes Ventolin® HFA (albuterol sulfate), and Schering-Plough, which makes Proventil® HFA (albuterol sulfate). In their comments to the agency, the companies estimated they would need up to 18 months to reach maximum production capacity after the FDA issues a definitive date for the phaseout. The FDA did not consider the impact of IVAX Laboratories Inc.'s albuterol HFA inhaler that was approved October 29, 2004, and introduced to the market in December 2004 because the product had been on the market such a short time.

The FDA said the new regulation is necessary because private markets are very unlikely to preserve levels of stratospheric ozone sufficient to protect the public health. Individual users of albuterol MDIs have no significant private incentive to switch to non-ozone depleting albuterol HFA MDIs. In fact, each user would bear all of the costs and virtually none of the benefits of such a switch, as the environmental and health benefits would tend to be distributed globally and occur decades in the future. Thus, the outcome of a private market would be continued use of the albuterol MDI available at the lowest price, even if the social value of reducing emissions were clearly much greater than the price premium for non-ozone depleting albuterol HFA MDIs.<sup>7</sup>

The FDA summarized the rule's objective to reduce atmospheric emissions of ODSs, specifically CFCs, and noted they "are ending the essential use designation for ODSs used in albuterol MDIs." It said removing this essential-use designation would comply with obligations under the Montreal Protocol and the Clean Air Act, thereby reducing emissions that deplete stratospheric ozone, while preserving access to essential drugs by minimizing adverse effects on affected patient populations.

To view the final rule, go to <http://www.fda.gov/OHRMS/DOCKETS/98fr/03p-0029.pdf>. For additional information, go to: <http://www.fda.gov/cder/mdi/default.htm>

## The Role of the Pharmacist in the Conversion

Albuterol MDIs are among the most widely used drug products for the treatment of asthma and COPD. Because of albuterol's rapid onset of action, albuterol MDIs are frequently used as "rescue" inhalers to treat bronchospasms during acute episodes. Albuterol MDIs can be considered life-saving for some patients at certain times and they are very important in controlling symptoms for many other patients. Because of the importance of these drugs, the seamless conversion of patients from CFC to HFA formulations is critical. Several studies have shown the positive impact the community pharmacist can have on outcomes with patients with asthma.<sup>8, 9, 10</sup> One project, a liaison council of the American College of Asthma, Allergy, and Immunology (ACAAI) and the American Pharmacists Association (APhA), has identified numerous areas for pharmacist involvement in optimal management of patients with asthma and allergies.<sup>11</sup> These include:

- Educating patients on their disease state;
- Counseling patients on the roles of their medications;
- Educating patients on the skills necessary to manage their medication use;
- Educating patients on environmental control measures that help to control asthma and allergies;
- Assessing the efficacy and tolerability of treatments;
- Monitoring adherence to therapy;
- Advising on nonprescription medications.

The pharmacist can play a key role in helping patients understand the differences between CFC and HFA inhalers including their dosing, cost, and other considerations.

## Asthma

Many Americans are affected by asthma, a serious chronic lung condition characterized by episodes or attacks of inflammation and narrowing of the small airways in response to asthma triggers. Over the past two decades, the burden of asthma in the United States has increased. However, within the last few years, mortality and hospitalizations due to asthma have decreased and asthma prevalence has stabilized, possibly indicating a higher level of disease management.<sup>12</sup> While asthma is a reversible obstructive lung disease, it can be life-threatening if not properly managed.<sup>13</sup>

Close to 20 million Americans had asthma in 2003, or about one in 15 people, including 6.2 million children. Of these, 11 million Americans (four million children under 18) had an asthma attack. Close to 1.9 million emergency room visits were attributed to asthma in 2002 and there were 4,261 deaths attributed to asthma.<sup>14</sup> In 2003, asthma accounted for an estimated 12.8 million lost school days in children and 24.5 million lost work days in adults. Asthma ranks within the top 10 prevalent conditions causing limitation of activity and costs our nation \$16.1 billion in healthcare costs annually, with \$11.5 billion in indirect costs (e.g., lost productivity) and another \$4.6 billion in

direct costs. Prescription drugs represented the largest single indirect cost, at \$5 billion. The value of lost productivity due to death represented the largest single indirect cost at \$1.7 billion.<sup>15</sup>

Asthma breathing problems usually happen in “episodes,” but the inflammation underlying asthma is continuous. An asthma episode is a series of events that result in narrowed airways. These include: swelling of the lining, tightening of the muscle, and increased secretion of mucus in the airway. The narrowed airway is responsible for the difficulty in breathing with the familiar “wheeze.”<sup>16</sup> Asthma medications help reduce underlying inflammation in the airways and relieve or prevent symptomatic airway narrowing. Control of inflammation should lead to reduction in airway sensitivity and help prevent airway obstruction.

Despite the numerous drugs available, asthma is still poorly controlled. One study reported that 72% of men and 86% of women with asthma had symptoms 15 years after they were first diagnosed with the disease. Only 19% of these people, however, were still seeing a doctor and only 32% used any medication to regularly manage their asthma.<sup>17</sup> A recent survey found that 48% of people with asthma say that the disease limits their ability to take part in sports and recreation, 36% say it limits their normal physical exertion, and 25% say it interferes with their social activities.<sup>18</sup>

### Asthma Treatment Guidelines

There are four components to asthma management, according to the Guidelines for the Diagnosis and Management of Asthma:<sup>19</sup>

- Measures of assessment and monitoring;
- Control of factors contributing to asthma severity;
- Pharmacologic therapy;
- Education for a partnership in asthma care.

One of the first things pharmacists can do to help patients with asthma is to help them understand common triggers and appropriate avoidance and control strategies.<sup>20</sup> Avoiding exposure to allergens with proven sensitivity, including common triggers, is important. So is avoiding exertion during high pollution periods.

Asthma can be characterized by the severity of symptoms as shown in Table 1.

Goals for asthma therapy include maintaining “near normal” pulmonary function, normal activity levels, preventing chronic or troublesome symptoms, providing optimal drug therapy with minimal or no adverse effects, and preventing recurrences and minimizing the need for ER visits or hospitalizations. Treatment is based upon a step approach, as is outlined in the guidelines.<sup>21</sup> Treatment should be reviewed every one to six months to see if a gradual stepwise reduction is possible. Conversely, if control is not maintained, then a step-up approach needs to be considered. The patient’s medication technique, adherence, and environmental control should be reviewed first, however. The usual doses of asthma medications used for quick relief are shown in Table 2.<sup>22</sup>

Pharmacists can play an important role in educating patients with the goal to help them take the actions needed to control their asthma. These actions include:

- Taking daily medications for long-term control as prescribed;
- Using delivery devices effectively—metered-dose inhalers, spacers, nebulizers;
- Identifying and controlling factors that make asthma worse;
- Monitoring peak flow and/or symptoms;
- Following the written action plan when symptoms or episodes occur.

A number of patient brochures are available through the *Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma 1997* treatment guidelines, including:

- What Everyone Should Know about Asthma Control
- How to Control Things that Make Your Asthma Worse
- How to Use Your Metered-Dose Inhaler the Right Way
- Asthma Action Plan
- School Self-Management Plan
- How to Use Your Peak Flow Meter

Most patients use their inhalers incorrectly, and this skill deteriorates over time. Patients’ poor technique results in less medication getting to the airways. The initial inhaler training can be done in minutes with the simple skills-training method:

1. **Tell** the patient the steps and give written instructions.
2. **Demonstrate** how to use the inhaler following each of these steps.
3. Ask the patient to **demonstrate** how to use the inhaler. Let the patient refer to the handout on the first training. Subsequently, use patient handouts as a checklist to assess the patient’s technique.
4. **Tell** patients what they did right and what they need to improve. Have them demonstrate their technique again, if needed. Focus the patient on improving one or two key steps (e.g., timing of actuation and inhalation) if the patient made multiple errors.

Long-term daily peak flow monitoring is recommended for those with moderate or severe persistent asthma or patients with a history of severe exacerbations. Pharmacists can also train patients to use their peak flow meter using the same four skills-training steps described for inhalers. Specific recommendations regarding peak flow monitoring include:

- Use the patient’s own personal best peak flow as the standard against which peak flow measurements should be compared;
- Use the same peak flow meter and, when needed, replace with same brand;
- Measure peak flow first thing in the morning before medications;
- A drop in peak flow below 80% of personal best indicates a need for added medications;
- A drop in peak flow below 50% of personal best

**TABLE 1.**  
**Classification of asthma severity**

**Clinical Features Before Treatment\***

	Symptoms**	Nighttime Symptoms	Lung Function
<b>STEP 4</b> Severe Persistent	<ul style="list-style-type: none"> <li>■ Continual symptoms</li> <li>■ Limited physical activity</li> <li>■ Frequent exacerbations</li> </ul>	Frequent	<ul style="list-style-type: none"> <li>■ FEV<sub>1</sub> or PEF ≤ 60% predicted</li> <li>■ PEF variability &gt; 30%</li> </ul>
<b>STEP 3</b> Moderate Persistent	<ul style="list-style-type: none"> <li>■ Daily symptoms</li> <li>■ Daily use of inhaled short-acting beta<sub>2</sub>-agonist</li> <li>■ Exacerbations affect activity</li> <li>■ Exacerbations ≥ 2 times a week; may last days</li> </ul>	> 1 time a week	<ul style="list-style-type: none"> <li>■ FEV<sub>1</sub> or PEF &gt; 60% – &lt; 80% predicted</li> <li>■ PEF variability &gt; 30%</li> </ul>
<b>STEP 2</b> Mild Persistent	<ul style="list-style-type: none"> <li>■ Symptoms &gt; 2 times a week but &lt; 1 time a day</li> <li>■ Exacerbations may affect activity</li> </ul>	> 2 times a month	<ul style="list-style-type: none"> <li>■ FEV<sub>1</sub> or PEF ≥ 80% predicted</li> <li>■ PEF variability 20% – 30%</li> </ul>
<b>STEP 1</b> Mild Intermittent	<ul style="list-style-type: none"> <li>■ Symptoms ≤ 2 times a week</li> <li>■ Asymptomatic and normal PEF between exacerbations</li> <li>■ Exacerbations brief (from a few hours to a few days); intensity may vary</li> </ul>	≤ 2 times a month	<ul style="list-style-type: none"> <li>■ FEV<sub>1</sub> or PEF ≥ 80% predicted</li> <li>■ PEF variability &lt; 20%</li> </ul>

\* The presence of one of the features of severity is sufficient to place a patient in that category. An individual should be assigned to the most severe grade in which any feature occurs. The characteristics noted in this figure are general and may overlap because asthma is highly variable. Furthermore, an individual's classification may change over time.

\*\* Patients at any level of severity can have mild, moderate, or severe exacerbations. Some patients with intermittent asthma experience severe and life-threatening exacerbations separated by long periods of normal lung function and no symptoms.

Source: National Institutes of Health—National Heart, Lung, and Blood Institute. Guidelines for the Diagnosis and Management of Asthma: Expert Panel Report 2. NIH publication 97-4051. July 1997. <http://www.nhlbi.nih.gov/guidelines/asthma/>

indicates a severe exacerbation.

It's important to remember that patients cannot be expected to perform a task they never agreed to do or one that is only mentioned once to them. Thus, two essential clinician activities for successful patient education are asking the patient for a verbal, sometimes written, agreement to take specific action(s) and following up and reinforcing the patient for the actions during subsequent visits or phone calls.

**COPD**

Although chronic obstructive pulmonary disease (COPD) and asthma share some clinical features, such as airflow obstruction, they are two distinct disorders, requiring distinct treatment approaches. COPD refers to two lung diseases, chronic bronchitis and emphysema, that are characterized by obstruction to airflow that interferes with normal breathing. Both of these conditions frequently co-exist; hence physicians prefer the term COPD. The disease is the fourth leading cause of death in America, claiming the lives of over 120,000 Americans in 2002.<sup>24</sup> Beginning in 2000, women have exceeded men in the number of deaths attributable to COPD. In 2002, over 61,000 females died compared with 59,000 males.<sup>25</sup> Smoking is the primary risk factor for COPD. Approximately 80% to 90% of COPD deaths are caused by smoking. Female smokers are

nearly 13 times as likely to die from COPD as women who have never smoked. Male smokers are nearly 12 times as likely to die from COPD as men who have never smoked.<sup>24</sup>

Other risk factors of COPD include air pollution, second-hand smoke, history of childhood respiratory infections, and heredity. Occupational exposure to certain industrial pollutants also increases the odds for COPD. A recent study found that the fraction of COPD attributed to work was estimated as 19.2% overall and 31.1% among never smokers.<sup>27</sup> In 2003, 10.7 million U.S. adults were estimated to have COPD.<sup>28</sup> However, close to 24 million U.S. adults have evidence of impaired lung function, indicating an under-diagnosis of COPD.<sup>29</sup> In 2004, the cost to the nation for COPD was approximately \$37.2 billion, including healthcare expenditures of \$20.9 billion in direct healthcare expenditures, \$7.4 billion in indirect morbidity costs, and \$8.9 billion in indirect mortality costs.<sup>30</sup> A recent American Lung Association survey revealed that half of all COPD patients (51%) say their condition limits their ability to work. It also limits them in normal physical exertion (70%), household chores (56%), social activities (53%), sleeping (50%), and family activities (46%).<sup>31</sup>

**COPD Treatment Guidelines**

A chronic cough is often the first symptom of COPD and

**TABLE 2.**  
Usual dosages for quick-relief medications

Medication	Dosage Form	Adult Dose	Child Dose*	Comments
<b>Short-acting Inhaled Beta<sub>2</sub>-Agonists</b>				
<i>MDI</i>				
Albuterol	90 mcg/puff, 200 puffs	2 puffs 5 minutes prior to exercise	1-2 puffs 5 minutes prior to exercise	<ul style="list-style-type: none"> <li>■ An increasing use or lack of expected effect indicates diminished control of asthma.</li> <li>■ Not generally recommended for long-term treatment. Regular use on a daily basis indicates the need for additional long-term-control therapy.</li> <li>■ Differences in potency exist, but all products are essentially comparable on a per puff basis. May double usual dose for mild exacerbation.</li> </ul>
Albuterol HFA	90 mcg/puff, 200 puffs	2 puffs tid-qid prn	2 puffs tid-qid prn	
Pirbuterol	200 mcg/puff, 400 puffs			
<i>DPI</i>				
Albuterol Rotahaler	200 mcg/capsule	1-2 capsules q 4-6 hours as needed and prior to exercise	1 capsule q 4-6 hours as needed and prior to exercise	
<i>Nebulizer solution</i>				
Albuterol	5 mg/mL (0.5%) 2.5 mg/3mL 1.25 mg/3mL 0.63 mg/3mL	1.25-5 mg in 3 cc of saline q 4-8 hours	0.05 mg/kg (min 1.25 mg, max 2.5 mg) in 3 cc of saline q 4-6 hours	<ul style="list-style-type: none"> <li>■ May mix with cromolyn or ipratropium nebulizer solutions. May double dose for severe exacerbations.</li> </ul>
Bitolterol	<i>Nebulizer solution</i> 2 mg/mL (0.2%)	0.5-3.5 mg (0.25-1 cc) in 2-3 cc of saline q 4-8 hours	Not established	<ul style="list-style-type: none"> <li>■ May not mix with other nebulizer solutions.</li> </ul>
<i>Nebulizer solution</i>				
Levalbuterol (R-albuterol)	0.31 mg/3mL 0.63 mg/3mL 1.25 mg/3mL	0.63 mg-2.5 mg q 4-8 hours	0.025 mg/kg (min. 0.63 mg, max. 1.25 mg) q 4-8 hours	<ul style="list-style-type: none"> <li>■ 0.63 mg of levalbuterol is equivalent in efficacy and side effects to 1.25 mg of racemic albuterol. The product is a sterile-filled preservative-free unit-dose vial.</li> </ul>
<b>Anticholinergics</b>				
<i>MDI</i>				
Ipratropium	18 mcg/puff, 200 puffs	2-3 puffs q 6 hours	1-2 puffs q 6 hours	<ul style="list-style-type: none"> <li>■ Evidence is lacking for anticholinergics producing added benefit to beta<sub>2</sub>-agonists in long-term-control asthma therapy.</li> </ul>
	<i>Nebulizer solution</i> 0.25 mg/mL (0.025%)	0.25 mg q 6 hours	0.25-0.5 mg q 6 hours	
<i>MDI</i>				
Ipratropium with albuterol	18 mcg/puff of ipratropium bromide and 90 mcg/puff of albuterol 200 puffs/canister	2-3 puffs q 6 hours	1-2 puffs q 8 hours	<ul style="list-style-type: none"> <li>■ Contains EDTA to prevent discoloration of the solution. This additive does not induce bronchospasm.</li> </ul>
	<i>Nebulizer solution</i> 0.5 mg/3 mL ipratropium bromide and 2.5 mg/3mL albuterol	3 mL q 4-6 hours	1.5-3 mL q 8 hours	
<b>Systemic Corticosteroids</b>			<b>(Applies to the first three corticosteroids)</b>	
Methylprednisolone	2-, 4-, 6-, 8-, 16-, 32-mg tablets	Short-course "burst": 40-60 mg/day as single or 2 divided doses for 3-10 days	Short-course "burst": 1-2 mg/kg/day, maximum 60 mg/day, for 3-10 days	<ul style="list-style-type: none"> <li>■ Short courses or "bursts" are effective for establishing control when initiating therapy or during a period of gradual deterioration.</li> <li>■ The burst should be continued until patient achieves 80% PEF personal best or symptoms resolve. This usually requires 3-10 days but may require longer. There is no evidence that tapering the dose following improvement prevents relapse.</li> <li>■ May be used in place of a short burst of oral steroids in patients who are vomiting or if adherence is a problem.</li> </ul>
Prednisolone	5-mg tablets, 5 mg/5cc, 15 mg/5 cc			
Prednisone	1-, 2.5-, 5-, 10-, 20-, 50-mg tablets; 5 mg/cc, 5 mg/5 cc			
<i>Repository Injection</i>				
(Methylprednisolone acetate)	40 mg/mL 80 mg/mL	240 mg IM once	7.5 mg/kg IM once	

\* Children ≤ 12 years of age.

**Source:** National Institutes of Health–National Heart, Lung, and Blood Institute. Global Initiative for Asthma: Global Strategy for Asthma Management and Prevention. NIH publication 02-3659. 2002.

may develop years before other symptoms occur. In addition to a productive cough, progressive dyspnea on exertion and impaired exercise intolerance are also present. As COPD progresses, the dyspnea and gas exchange worsens, resulting in a further negative cycle where patients become disconditioned due to lack of exercise which makes their dyspnea worse.<sup>32</sup> The quality of life for a person suffering from COPD diminishes as the disease progresses. At the onset, there is minimal shortness of breath. People with COPD may eventually require supplemental oxygen and may have to rely on mechanical respiratory assistance.<sup>33</sup>

Pharmacists can help improve adherence for patients with COPD using treatment guidelines. Two are the NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria and the American Thoracic Society (ATS)/European Respiratory Society criteria.<sup>34, 35</sup> Both guidelines offer evidence-based strategies to assess and monitor COPD, reduce risk factors, manage stable COPD, and treat exacerbations.

COPD is not curable, and many of its symptoms are irreversible. The GOLD and the newer ATS/ERS criteria use postbronchodilatory spirometry measurements to stage severity. Stage I (mild) is defined as a postbronchodilatory FEV<sub>1</sub> of  $\geq 80\%$  of predicted value. The ratio of FEV<sub>1</sub>/FVC is  $< 70\%$  for Stages I to IV of COPD. Symptoms may or may not be present. Stage II (moderate) is characterized by worsening airflow and a postbronchodilatory FEV<sub>1</sub> of between 50% and 79% of predicted values. In Stage III (severe), further worsening occurs and postbronchodilatory FEV<sub>1</sub> deteriorates to between 30% and 49% of predicted values. Finally, Stage IV (very severe) is defined as postbronchodilatory FEV<sub>1</sub> less than 30% of predicted value, with or without symptoms.

Prevention is the number one goal, particularly for patients identified in Stage 0. Non-pharmacological therapies used in managing COPD include smoking cessation, immunizations to prevent respiratory infections, pulmonary rehabilitation programs, and oxygen therapy. The maintenance treatment of COPD utilizes a step-up approach with therapies added as the disease progresses and the severity of symptoms increases. Regular treatment must be maintained at the same level for long periods of time, with adjustment made as needed to treat disease progression and/or side effects. Because no existing medication is currently known to modify the long-term decline in lung function that is characteristic of COPD, therapy is aimed at decreasing symptoms and complications.

For patients in Stage I (mild), the addition of a short-acting bronchodilator, such as albuterol or ipratropium, is recommended on an as-needed basis. For patients in Stage II (moderate), regular treatment with a long-acting bronchodilator is recommended, with supplemental use of a short-acting bronchodilator for rescue. Long-acting beta<sub>2</sub>-agonists, such as inhaled formoterol and salmeterol, have a duration of action  $\geq 12$  hours and require twice-daily dosing. Inhaled ipratropium bromide is a short-acting anticholinergic with a duration of action of six to eight hours.

Tiotropium bromide has a duration of action  $\geq 24$  hours and requires once-daily dosing. A combination of short-acting beta<sub>2</sub>-agonists and an anticholinergic agent is also recommended at this stage, since combining drugs with different mechanisms may increase the degree of bronchodilation achieved without increasing side effects. Single drugs may be administered in combination, or a combination product may be used. In the United States, albuterol and ipratropium are available as a combination product. Regular treatment with more than one long-acting bronchodilator may be needed for patients in this stage of COPD. Oral theophylline may also be used in Stage II, although it is less preferred because of its associated risks of toxicity.

For patients in Stage III (severe), the addition of inhaled corticosteroid (ICS) agents as part of regular maintenance therapy is recommended if the patient experiences repeated exacerbations while receiving bronchodilator therapy. ICS agents include beclomethasone, fluticasone, and triamcinolone. For patients requiring both a bronchodilator and ICS agents, a combination product of fluticasone/salmeterol is available. Finally, for patients in Stage IV (very severe), the administration of long-term oxygen is recommended if the patient experiences chronic respiratory failure. Continuous-oxygen therapy,  $> 15$  hours per day, has been shown to increase survival in patients with chronic respiratory failure.<sup>36</sup>

Bronchodilator drugs commonly used in treating COPD are depicted in Table 3.

The choice depends on the availability of the medication and the patient's response. The GOLD guidelines report that all categories of bronchodilators have been shown to increase exercise capacity in COPD. Regular treatment with long-acting bronchodilators is more effective and convenient than treatment with short-acting bronchodilators, but more expensive. Regular use of a long-acting beta<sub>2</sub>-agonist or long-acting anticholinergic improves health status. Theophylline is effective in COPD, but due to its potential toxicity, inhaled bronchodilators are preferred when available. All studies that have shown efficacy of theophylline in COPD were done with slow-release preparations.

Combining drugs with different mechanisms and durations of action might increase the degree of bronchodilation for equivalent or lesser side effects. A combination of a short-acting beta<sub>2</sub>-agonist and an anticholinergic produces greater and more sustained improvements in FEV<sub>1</sub> than either alone and does not produce evidence of tachypylaxis over 90 days of treatment. Combination of a beta<sub>2</sub>-agonist, an anticholinergic, and/or theophylline may produce additional improvements in lung function, and health status. Increasing the number of drugs usually increases costs, and an equivalent benefit may occur by increasing the dose of one bronchodilator when side effects are not a limiting factor. Increasing the dose of either a beta<sub>2</sub>-agonist or an anticholinergic, especially when given by a wet nebulizer, appears to provide subjective benefit in acute episodes.

As with asthma, pharmacists are in a position to play a key role in the management of patients with COPD. Helping patients understand the importance of smoking cessation and offering programs to do so is important. Smoking cessation is the single most effective intervention to reduce the risk of developing COPD and the only intervention that has been shown to slow its progression. If a pharmacist doesn't offer a program directly, he or she should determine which smoking cessation resources are available in the community and make this information available to patients. Inhalation therapy is a cornerstone of treatment. Teaching patients proper inhalation techniques as outlined earlier is important. COPD is amenable to therapy. A management strategy consisting of combined pharmacotherapy and non-pharmacotherapeutic interventions can effectively improve symptoms, activity levels, and quality of life, even in patients with severe COPD.

### The Move from CFCs to HFAs

As a review of asthma and COPD treatment guidelines shows, MDIs are among the most effective therapeutic treatment for these diseases. MDIs have been in use for 45 years; the first MDI product (3M Riker's Medihaler Epi™) was introduced in 1956. MDIs account for about 70% of all inhalation therapy.<sup>37</sup> MDIs have a long history of patient acceptance, physician confidence, pharmacoeconomic benefits, and regulatory approvals and have resulted in improved quality of life for millions of people throughout the world. MDIs allow for targeted delivery of the drug to the desired site of the therapeutic effect, allowing delivery of therapeutically effective local levels of drug to the target tissues in the lung with limited systemic exposure.

Yet, from a drug delivery perspective, traditional CFC-based MDIs are inefficient, delivering only about 5% to 25% of the drug to the lung.<sup>38</sup> The transition to HFA propellants has caused many current and prospective manufacturers of MDI inhalers to research advances in MDI technology (Figure 2). This research has resulted in highly efficient MDI systems that are broadly applicable to treating a wide variety of diseases beyond traditional lung ailments. The technical improvements include all aspects of MDI systems: formulations, valves, canisters, elastomers, mouthpieces, etc.

Pharmacists should be aware that these technical changes have led to greatly improved therapeutic benefits, including dosing consistency, less temperature sensitivity, optimal dose release during inhalation, and longer shelf life.<sup>39, 40, 41</sup> For example, changes to valve design provide dosing consistency. In one study, after a full week of storage, the improved HFA MDI provided uniform dosing, whereas the older CFC MDI gave erratic dosing after only hours of storage. Another difference between HFA inhalers and their CFC counterparts is their temperature sensitivity with HFA MDIs less sensitive to temperature due to the higher volatility of HFA propellants. These new HFA propellants are capable of significantly improved drug deliv-

**TABLE 3.**

### Bronchodilators commonly used in treating COPD

#### Beta<sub>2</sub>-agonists

Short-acting  
Albuterol  
Terbutaline  
Long-acting  
Formoterol  
Salmeterol

#### Anticholinergics

Short-acting  
Ipratropium bromide  
Long-acting  
Tiotropium

#### Combination short-acting beta<sub>2</sub>-agonists plus anticholinergic in one inhaler

Albuterol/Ipratropium

#### Methylxanthines

Aminophylline (slow-release preparations)  
Theophylline (slow-release preparations)

#### Inhaled glucocorticosteroids

Beclomethasone  
Budesonide  
Fluticasone  
Triamcinolone

#### Combination long-acting beta<sub>2</sub>-agonists plus glucocorticosteroids in one inhaler

Formoterol/Budesonide  
Salmeterol/Fluticasone

#### Systemic glucocorticosteroids

Prednisone  
Methylprednisolone

ery efficiency compared with CFC MDIs or conventional dry powder inhalers (DPIs.) Key differences between CFC and HFA propellants are shown in Table 4.<sup>42</sup>

These differences have been shown in studies as well. For example, patients in a large (n = 323) blinded study were given doses of beclomethasone dipropionate (BDP) ranging from 100 to 800 mcg/day using either the CFC-BDP MDI or the HFA-BDP MDI formulations. The results from this study indicated that higher doses of the CFC-BDP (approximately 2.6 times higher) were needed in order to produce equivalent improvement in FEV<sub>1</sub> compared with lower doses of the HFA-BDP.<sup>43</sup> This study demonstrates that HFA MDIs are capable of reducing the dose required to treat lung diseases, such as asthma, thus reducing the potential for side effects.

HFAs are generally similar to CFCs in terms of patient safety and efficacy. There are some specific differences, however, between the CFC and HFA inhalers that are product dependent and generally center on priming the inhaler. Pharmacists should counsel patients accordingly per the manufacturer instructions outlined in Table 5.

Most of the drugs available as CFC products have been

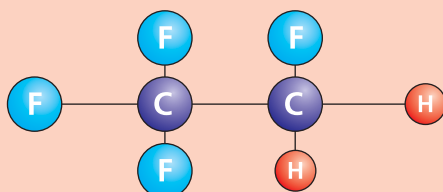
**TABLE 4.**  
Physical differences between CFC and HFA propellants

Parameter	CFC Formulation	HFA Formulation
Taste	Differs from HFA—"harder"	Differs from CFC—"softer"
Spray volume	Higher	Lower
Spray force	Higher	Lower by about one-third
Spray temperature	Lower	Higher (86° F)
Dose delivery from nearly empty canister	Erratic	More consistent
Dose delivery under different temperatures	Variable	More consistent

Source: Tscheng DZ. CPJ/RPC 2002;21-24. [http://www.pharmacists.ca/content/cpjpdfs/june02/alternatives\\_to\\_CFCcontainingMDIs.pdf](http://www.pharmacists.ca/content/cpjpdfs/june02/alternatives_to_CFCcontainingMDIs.pdf). Accessed August 25, 2005

**FIGURE 2**  
HFA: An alternative to CFC

- A very low chemical reactivity
- Nonflammable gas
- Low water and lipid solubility
- Does not deplete ozone layer
- Low order of toxicity



reformulated and launched as HFAs with the exception of terbutaline and formoterol. The overall cost to the industry related to the CFC-to-HFA transition globally was estimated at \$1 billion U.S. in 1999.

### FDA Orange Book Ratings and Product Substitution

HFA-propellant formulations of inhaled drugs are not generically interchangeable with their CFC counterparts nor across their HFA counterparts. Specifically, none of the albuterol sulfate HFA products are AB rated in the FDA Orange Book ([www.fda.gov/cder/ob](http://www.fda.gov/cder/ob)); rather they are BX rated. Drug products that FDA considers not to be therapeutically equivalent to other pharmaceutically equivalent products, (i.e., drug products for which actual or potential bioequivalence problems have not been resolved by adequate evidence of bioequivalence) are designated BC, BD, BE, BN, BP, BR, BS, BT, BX, or B\*. Often the problem is with specific dosage forms rather than with the active ingredients. Specifically, a BX code is assigned to specific drug products for which the data that have been reviewed by the agency are insufficient to determine therapeutic equivalence under the policies stated in this document. In these situations, the drug products are presumed to be *therapeutically inequivalent* until the agency

has determined that there is adequate information to make a full evaluation of therapeutic equivalence.

The practical impact of the BX rating is that the three available albuterol sulfate HFA inhalers are not generically substitutable for one another nor are they substitutable for their CFC counterpart. As such, physicians writing prescriptions should specify either Albuterol HFA, Proventil HFA, or Ventolin HFA. Product substitution laws vary state by state. As a result, while generic substitution is not permissible when the FDA Orange Book ratings are used, some states might have different substitution guidelines. As such, pharmacists are encouraged to revisit their state product substitution laws related to BX-rated products.

### Steps for Patients in Converting Inhalers

There are a number of important factors to consider when patients convert from CFC-to-HFA inhalers, including possible dosing adjustments, differing spray characteristics that may impact patient perception and inhaler use, and cost considerations.

While most new HFA inhaler formulations are comparable in safety and efficacy to their CFC counterparts, there may be instances where dosing adjustments for patients are required. This is because HFA formulation MDIs are more efficient at drug delivery than their counterparts. Pharmacists should counsel patients to carefully self-monitor their conditions. If the medicine seems to become less effective, if patients' condition worsens, or they begin to experience side effects, they should be advised to see their physician to assess whether dosage adjustments may be necessary. It is important to let patients know that HFA is an inert propellant and it has not been shown to interact with active ingredients in inhalers or to cause any other side effects.

Patients switching to the HFA formulations may notice a softer and warmer spray with a slightly different, possibly bitter, taste or inhalation sensation than the CFC version of their medication. It is critical to educate patients before they begin using the HFA inhalers about these differences because the patient may perceive they are "not getting the dose" and use more puffs than necessary causing possible adverse reactions and product waste. Spacers can also be used with HFA formulations.

**TABLE 5.**  
**HFA inhalers: Specific patient instructions\***

Product	Manufacturer	Adult Dosing	Priming Required	Usage Notes
<b>Short-Acting Beta<sub>2</sub>-Agonists</b>				
Albuterol				
Albuterol HFA 8.5 grams, 200 metered doses	IVAX Laboratories, Inc.	2 puffs every 4-6 hours; each puff delivers 90 mcg albuterol base	3 Test Sprays before use and after no use for 2 weeks	Shake well before use; Clean mouthpiece weekly
Proventil HFA 6.7 grams, 200 metered doses	Key Pharmaceuticals	2 puffs every 4-6 hours; each puff delivers 90 mcg albuterol base	4 Test Sprays before use and after no use for 2 weeks	Shake well before use; Clean mouthpiece weekly
Ventolin HFA 18 grams, 200 metered doses	GlaxoSmithKline	2 puffs every 4-6 hours; each puff delivers 90 mcg albuterol base	4 Test Sprays before use and after no use for 2 weeks	Shake well before use; Clean mouthpiece weekly
<b>Anticholinergics</b>				
Ipratropium				
Atrovent HFA 12.9 grams, 200 metered doses	Boehringer Ingelheim	2 puffs, 4 times a day; each puff delivers 17 mcg ipratropium	2 Test Sprays before use and after no use for 3 days	Does not require shaking; Clean mouthpiece weekly
<b>Corticosteroids</b>				
Beclomethasone				
QVAR HFA 40 mcg, 7.3 grams; 100 metered doses 80 mcg, 7.3 grams; 100 metered doses	IVAX Laboratories, Inc.	40-80 mcg 2 times a day; depending on use of other agents	2 Test Sprays before use and after no use for 10 days	Does not require shaking; Clean mouthpiece weekly
Fluticasone				
Flovent HFA 44mcg, 10.6 grams, 120 metered doses 110 mcg, 12 grams, 120 metered doses, 220 mcg, 12 grams, 120 metered doses	GlaxoSmithKline	88mcg-440 mcg 2 times a day depending on use of other agents	4 Test Sprays before use and after no use for 7 days or if dropped	Shake well before use; Clean mouthpiece weekly
Triamcinolone				

\* Information compiled from each product's prescribing information leaflet accessed via the Internet on August 25, 2005.

There are also cost implications for converting patients from CFC- to HFA-based inhalers as well since the three available albuterol sulfate HFA-based inhalers are not substitutable with the generic CFC formulation and each carries a higher average wholesale price. AWP for Albuterol HFA is \$36.72, \$43.96 for Proventil HFA, and \$37.63 for Ventolin HFA.<sup>44</sup> FDA carefully considered cost issues in its decision on when to phase out CFC-based albuterol inhalers. Detailed economic analyses were conducted because the rule will increase spending for needed albuterol medications until generic HFA versions reach the market. FDA estimates that the switch will cost between \$6.2 billion-\$8.3 billion (depending on annual discount rates assumed) in today's dollars for the period December 31, 2008, to December 2017 when the first generic albuterol HFA inhaler will become available. The agency assumed the retail cash price per albuterol MDI would rise by \$27. Eleven percent of the overall cost

increase, or \$95 annually per person, was estimated to be paid by uninsured patients. Representatives from both GlaxoSmithKline and Schering Laboratories told the FDA at the June 2004 advisory committee meeting and in subsequent comments that their patient assistance programs would be covering some low-income inhaler users (two million inhalers for GSK) and in GSK's instance, it would also be distributing at least three million \$10-off coupons for its product. These programs led FDA to say in its rulemaking, "We believe that the programs can, if properly utilized, provide a safety net for lower-income patients who otherwise could not afford this very important drug." It is important to note that the FDA's cost estimates did not include the impact of IVAX Laboratories Inc.'s albuterol HFA because it was too new to the market when the rule was promulgated. The IVAX Laboratories Inc. product carries the lowest cost of the three albuterol HFA inhalers on the market.

While insurers are expected to cover new HFA formulations, it is not known if they will move them to a different formulary co-payment tier because generic substitutes are no longer available. For patients who have financial issues, pharmacists should work with them to see if they may access any patient assistance CE programs. The Pharmaceutical Research and Manufacturers of America (PhRMA), along with many coalition partners, operates a coordinated Web site that allows patients to determine their eligibility for manufacturer and state assistance programs. The Web site is [www.pparx.org](http://www.pparx.org). If the patient does not qualify for any programs, pharmacists may want to work with their physician caregivers to see if there are any suitable alternative medications, which may be available generically.

### Pharmacist Counseling Tips

In summary, for the most part, patients switching from CFC- to HFA-based inhaler formulations should experience little change. A quick "Your Questions Answered" fact sheet from August 5, 2004, may also be accessed at [http://www.yourlunghealth.org/headlines/cfc\\_inhalers\\_qa.cfm](http://www.yourlunghealth.org/headlines/cfc_inhalers_qa.cfm) or [www.yourlunghealth.org/headlines/cdc\\_inhalers\\_qa.cfm](http://www.yourlunghealth.org/headlines/cdc_inhalers_qa.cfm). It outlines the reasons behind the CFC phaseout; how the new inhalers compare with the older ones; and addressing

some cost, insurance, and access issues. Pharmacists should advise patients:

- that HFA sprays tend to have a slightly different taste and inhalation sensation than their CFC counterparts. Patients may not perceive they are getting the right amount of medication because of the spray differences.
- the spray is softer and warmer, avoiding the "cold spray effect" associated with CFC inhalers.
- about priming their inhalers as some HFA formulations will require different priming than their CFC counterparts. Pharmacists should become familiar with each formulation and advise patients accordingly.
- that the HFA and CFC formulations for each inhaler and drug are comparable in efficacy and safety.
- that HFA is an inert propellant that does not interact with the active ingredient in inhalers or cause any other side effects.
- they should avoid spraying HFA formulations in their eyes, as with their CFC counterparts.
- if their medication seems to become less effective or if asthma worsens, they should seek immediate medical attention. □

### References

1. Morrisette, PM. *Natural Resources Journal*. 1989; 29:793-820.
2. FDA 21 CFR Part 2 Docket No. 2003-0029. Use of Ozone-Depleting Substances; Removal of Essential-Use Designations. March 31, 2005 Federal Register.
3. Ibid.
4. Colthorpe P. Industry Experiences of the HFA Transition. *DDS&S*. 2003;3:41-43.
5. United Nations Environmental Programme, "Production and Consumption of Ozone-Depleting Substances 1986-2000," 2002.
6. U.S. Environmental Protection Agency, "The Benefits and Costs of the Clean Air Act: 1990-2010" (<http://www.epa.gov/airsect812/copy99.html>).
7. Ibid 3.
8. Cordina, M et al. Assessment of a Community Pharmacy-Based Program for Patients with Asthma *Pharmacotherapy* 2001; 21(10):1196-1203.
9. Pauley TR et al. Pharmacist-Managed, Physician-Directed Asthma Management Program Reduces Emergency Department Visits. *Ann Pharmacother* 1995;29:5-9.
10. McLean W et al. The BC Community Pharmacy Asthma Study: A Study of Clinical, Economic and Holistic Outcomes Influenced by an Asthma Care Protocol Provided by Specially Trained Community Pharmacists in British Columbia. *Can Respir J*. 2003;10:195-202.
11. Marshik, P. Pharmacists and Allergists: Working Together to Improve the Management of Patients With Asthma and Allergies *J Am Pharm Assoc* 2003;3:439-440.
12. Trends in Asthma Morbidity and Mortality. American Lung Association. May 2005. <http://www.lungusa.org/atf/cf/%7B7A8D42C2-FCCA-4604-8ADE-7F5D5E762256%7D/ASTHMA1.PDF>. Accessed August 23, 2005.
13. National Institutes of Health-National Heart, Lung, and Blood Institute. Global Initiative for Asthma: Global Strategy for Asthma Management and Prevention. NIH publication 02-3659. 2002.
14. National Center for Health Statistics. Report of Final Mortality Statistics, 2002
15. National Heart, Lung and Blood Institute Chartbook, U.S. Department of Health and Human Services, National Institute of Health, 2004. <http://www.nhlbi.nih.gov/resources/docs/cht-book.htm> Accessed August 24, 2005.
16. National Institutes of Health-National Heart, Lung, and Blood Institute. Guidelines for the Diagnosis and Management of Asthma: Expert Panel Report 2. NIH publication 97-4051. July 1997. <http://www.nhlbi.nih.gov/guidelines/asthma/>
17. Clark NM, Partridge MR. Strengthening asthma education to enhance disease control. *Chest*. 2002;121:1661-1669.
18. Asthma in America Survey Project 1998. Glaxo Smith Kline.
19. National Institutes of Health-National Heart, Lung, and Blood Institute. Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma: Update on Selected Topics 2002. NIH publication 02-5075. June 2002. <http://www.nhlbi.nih.gov/guidelines/asthma/>
20. Ibid 16
21. Ibid 18
22. Ibid
23. Ibid
24. National Center for Health Statistics. Report of Final Mortality Statistics, 2002.
25. Ibid
26. U.S. Department of Health and Human Services. *The Health Consequences of Smoking*. A Report of the Surgeon General, 2004.
27. Hnizdo E., Sullivan, PA, Bang KM and G. Wagner. Association between COPD and Employment by Industry and Occupation in the US Population: A Study of Data from the Third National Health and Nutrition Examination Survey. *American Journal of Epidemiology*. 2002;156:8.
28. Chronic Bronchitis and Emphysema Morbidity and Mortality Trend Report. May 2005. American Lung Association. <http://www.lungusa.org/atf/cf/{7A8D42C2-FCCA-4604-8ADE-7F5D5E762256}/COPD1.pdf>. Accessed August 24, 2005.
29. Mannino DM, Homa DM, Akinbami L, et al. Chronic Obstructive Pulmonary Disease Surveillance - U.S., 1997-2000. *Morbidity and Mortality Weekly Report*. Vol. 51 (SS06); 1-16.
30. Ibid 14
31. Confronting COPD in America, 2000. Schulman, Ronca and Bucuvalas, Inc. (SRBI) Funded by Glaxo Smith Kline.
32. American Thoracic Society. Standards for the Diagnosis and Management of Patients with COPD; 2004. [www.thoracic.org/COPD](http://www.thoracic.org/COPD). Accessed August 24, 2005.
33. Global Initiative for Chronic Obstructive Pulmonary Disease. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease, 2003. [www.goldcopd.com](http://www.goldcopd.com). Accessed August 24, 2005.
34. Ibid 31
35. Ibid 30
36. Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy group in hypoxemic chronic obstructive lung disease: a clinical trial. *Ann Intern Med*. 1980;93:391-398.
37. Ibid 4
38. Stein SW, Steffely JS. Reinventing Metered Dose Inhalers: From Poorly Efficient CFC MDIs to Highly Efficient HFA MDIs. *Drug Delivery Technology*. <http://www.drugdeliverytech.com/cgi-bin/articles.cgi?idArticle=112> Accessed August 25, 2005
39. Ross D, Carlson S, June D. Comparison of A New HFA Albuterol Metered Dose Inhaler (MDI) To A Marketed CFC Albuterol MDI - Effect Of Storage Orientation, End Of Canister Life, And Temperature On Dosing Consistency. *Am J Respir Crit Care Med*. 1996;153:A62.
40. Clark AR. Metered Atomisation for Respiratory Drug Delivery. PhD Thesis for Department of Mechanical Engineering, Loughborough University, Loughboro, UK; 1991.
41. Clark AR. The Physics Of Aerosol Formation By Mdis - Limitations Of The Current Approach. *J Biopharm Sciences*. 1992;3:069-076.
42. Tscheng DZ. CPI/RPC 2002;21-24. [http://www.pharmacists.ca/content/cpi/dfs/june02/alternatives\\_to\\_CFC-containingMDIs.pdf](http://www.pharmacists.ca/content/cpi/dfs/june02/alternatives_to_CFC-containingMDIs.pdf) Accessed August 25, 2005
43. Busse W, Colice G, Hannon, S. CFC-BDP Requires 2.6 Times The Dose To Achieve Equivalent Improvement In FEV1 As HFA-BDP. *Am J Respir Crit Care Med*. 1998;49:A405.
44. Accessed AWP pricing from FirstDataBank loaded in PDX pharmacy system August 25, 2005.

# The Impact of CFC-to-HFA Conversion

## What Pharmacists Need to Know

### Self-Assessment Questions

Write your answers on the answer form appearing on page 16 (photocopies of the answer form are acceptable) or on a separate sheet of paper. Mark the most appropriate answer.

- The Food & Drug Administration issued a final regulation on March 31, 2005, that requires the phase-out of all CFC albuterol metered-dose inhalers by December 31, 2008.
  - True
  - False
- Excessive exposure to solar radiation is associated with adverse health effects, including:
  - Skin cancer
  - Cataracts
  - Arthritis
  - Asthma
  - A and B
- CFCs that are used in solvents and propellants are gradually broken down by strong ultraviolet light in the stratosphere, where they release chlorine atoms that then deplete ozone. The global environmental problem of stratospheric ozone depletion culminated in the Montreal Protocol, an international agreement to regulate and reduce production of ozone-depleting substances.
  - True
  - False
- Which of the following statements is false?
  - 186 countries have now ratified the Montreal Protocol.
  - The overall usage of CFCs has been dramatically reduced because of the Montreal Protocol.
  - Each year, countries party to the Montreal Protocol decide how much CFCs they need for "essential use."
  - Almost all the CFCs in inhalers are released into the environment upon exhalation.
  - EPA estimates the value of a "fully implemented" Montreal Protocol to be \$100 million between 1990 and 2165.
- In establishing a December 31, 2008, phaseout of CFC-based inhalers, the FDA used the following criteria:
  - At least two non-CFC products with the same active drug would be on the market for the same indication
  - Supplies and production capacity for non-CFC products will exist by December 31, 2008, at levels sufficient to meet patient needs
  - Adequate U.S. postmarketing use data are available for the non-CFC product
  - All of the above
- The pharmacist can play a key role in helping patients understand the differences between CFC and HFA inhalers. Some important points to convey include:
  - Any dosage differences
  - Differences in spray characteristics
  - Cost considerations in choosing products
  - Generic availability and interchangeability between all HFA products
  - A, B, and C
- Albuterol MDIs are often used as "rescue" inhalers to treat bronchospasms with acute asthma and allergies. Because of the "life-savings" aspect of this therapy, seamless conversion of patients from CFC MDIs to HFA MDIs is even more important.
  - True
  - False
- Pharmacists can play a number of roles in optimal management of patients with asthma and allergies. Which of the following is not one?
  - Educating patients about their disease state
  - Counseling patients on the roles of their medications
  - Teaching patients skills necessary to manage their medication use
  - Converting patients from HFA to CFC inhalers
  - Monitoring medication therapy and encouraging adherence
- Which of the following statements about asthma is false?
  - The prevalence of asthma has declined in the U.S. during the past two decades.
  - Close to 20 million Americans had asthma in 2003, or about one in 15 people.
  - Close to 1.9 million emergency room visits were attributed to asthma in 2002.
  - In 2003, asthma accounted for an estimated 12.8 million lost school days in children and 24.5 million lost work days in adults.
  - Asthma ranks within the top 10 prevalent conditions causing limitation of activity and costs our nation \$16.1 billion in healthcare costs annually.
- Which of the following are among the four components to asthma management, according to the Guidelines for the Diagnosis and Management of Asthma:
  - Measures of assessment and monitoring
  - Control of factors contributing to asthma severity
  - Pharmacologic therapy
  - Education for a partnership in asthma care
  - All of the above
- Which of the following are goals for asthma therapy?
  - Maintaining "near normal" pulmonary function
  - Preventing chronic or troublesome symptoms
  - Providing optimal drug therapy with minimal or no adverse effects
  - Preventing recurrences and minimizing the need for ER visits or hospitalizations.
  - All of the above
- COPD refers to two lung diseases, chronic bronchitis and emphysema, that are characterized by obstruction to airflow that interferes with normal breathing.
  - True
  - False
- Which of the following statements about COPD is false?
  - It is the fourth leading cause of death in America, claiming the lives of over 120,000 Americans in 2002.
  - In 2004, the cost to the nation for COPD was approximately \$37.2 billion.
  - Smoking is not a significant contributor to COPD deaths.
  - Risk factors for COPD include air pollution, second-hand smoke, history of childhood respiratory infections, and heredity.
  - Occupational exposure to certain industrial pollutants increases the odds for COPD.
- Treatment for both asthma and COPD treatment is based upon a step approach to therapy.
  - True
  - False

15. Which of the following statements are true?
- COPD is not curable, and many of its symptoms are irreversible.
  - Asthma is a reversible obstructive lung disease.
  - Step therapy for asthma is reassessed every one to six months.
  - COPD is characterized by "stages" defined by a patient's FEV.
  - All of the statements are true.

16. Pharmacists can play key roles in the management of patients with COPD, including:
- Helping patients understand the importance of smoking cessation
  - Offering smoking cessation programs or referring patients to those offered in the community
  - Teaching patients proper inhalation techniques since inhalation therapy is a cornerstone of treatment
  - All of the above

17. The transition to HFA propellants has caused many current and prospective manufacturers of MDI inhalers to research advances in MDI technology.
- True
  - False

18. Which of the following is not among the technological advances in MDI inhalers?
- better dosing consistency
  - more temperature sensitivity
  - optimal dose release during inhalation
  - longer shelf life

19. Which of the following is false about HFA inhalers as compared with CFC inhalers?
- They have a softer spray.
  - They use a higher spray volume.
  - They may be more costly.
  - They have a higher spray temperature.

20. Key counseling messages for pharmacists to patients on converting from CFC to HFA inhalers include:
- HFA sprays tend to have a slightly different taste and inhalation sensation than their CFC counterparts
  - The spray is softer and warmer, avoiding the "cold spray effect" associated with CFC inhalers
  - Priming instructions should be given as some HFA formulations will require different priming than their CFC counterparts
  - The HFA and CFC formulations for each inhaler and drug are comparable in efficacy and safety
  - All of the above

### Continuing Education Accreditation

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### Answer Form

December 12, 2005 UPN 012-999-05-223-HO1. Test questions start on page 15.

### The Impact of CFC-to-HFA Conversion: What Pharmacists Need to Know

- |   |  |  |  |
|---|--|--|--|
| 1. <input type="radio"/> a. <input type="radio"/> b.  | 6. <input type="radio"/> a. <input type="radio"/> b. <input type="radio"/> c. <input type="radio"/> d. <input type="radio"/> e.  | 11. <input type="radio"/> a. <input type="radio"/> b. <input type="radio"/> c. <input type="radio"/> d. <input type="radio"/> e. | 16. <input type="radio"/> a. <input type="radio"/> b. <input type="radio"/> c. <input type="radio"/> d.                          |
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| 3. <input type="radio"/> a. <input type="radio"/> b.  | 8. <input type="radio"/> a. <input type="radio"/> b. <input type="radio"/> c. <input type="radio"/> d. <input type="radio"/> e.  | 13. <input type="radio"/> a. <input type="radio"/> b. <input type="radio"/> c. <input type="radio"/> d. <input type="radio"/> e. | 18. <input type="radio"/> a. <input type="radio"/> b. <input type="radio"/> c. <input type="radio"/> d.                          |
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- |   |                |   |   |                   |
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