

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
OFFICE OF DIRECTOR

ACTION REFERRAL

TO <i>Grise</i>	DATE  <i>4-18-12</i>
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<p style="text-align: center;"><b>DIRECTOR'S USE ONLY</b></p> <p>1. LOG NUMBER  <i>000401</i></p> <p>2. DATE SIGNED BY DIRECTOR  </p>	<p style="text-align: center;"><b>ACTION REQUESTED</b></p> <p><input type="checkbox"/> I Prepare reply for the Director's signature DATE DUE _____</p> <p><input type="checkbox"/> I Prepare reply for appropriate signature DATE DUE _____</p> <p><input type="checkbox"/> I FOIA DATE DUE _____</p> <p><input checked="" type="checkbox"/> Necessary Action</p>
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APPROVALS <small>(Only when prepared for director's signature)</small>	APPROVE	* DISAPPROVE <small>(Note reason for disapproval and return to preparer.)</small>	COMMENT
1.			
2.			
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...adding tomorrows every day.

*Greene/04*

April 10, 2012

**RECEIVED**

**APR 17 2012**

Department of Health & Human Services  
OFFICE OF THE DIRECTOR

Mr. Anthony Keck  
Director of Medicaid  
Department of Health & Human Services  
1801 Main Street PO Box 8206  
Columbia, SC 29201-8206

Dear Mr. Keck,

On behalf of patients and families with cystic fibrosis (CF), we write to urge your state Medicaid program to utilize the new HCPCS code, J7131, established by Centers for Medicare and Medicaid Services (CMS) for the reimbursement of hypertonic saline products. CMS declared HCPCS code J7131 for "hypertonic saline solution, 1 mL" effective as of January 1, 2012. To further explain this issue, we have attached a comprehensive clinical bulletin on hypertonic saline products for your review.

Cystic fibrosis (CF) is an inherited, life-threatening disease that affects the lungs and digestive systems of about 30,000 children and adults in the United States. Nearly half of all children with CF and one in three adults rely on Medicaid to receive the specialized care needed to stay healthy. Because the lives of CF patients are severely impacted by a steady decline in lung function, the preservation of lung function is central to CF care.

Regular use of inhaled hypertonic saline (HS) can improve lung function in people with CF and is recommended by the Cystic Fibrosis Foundation for use in individuals with CF who are at least 6 years old. Aerosolized HS thins the mucus found in the lungs of CF patients. This allows patients to more easily clear their lungs, lessening the likelihood of contracting lung infections that require costly antibiotics and hospitalizations. In addition to preventing costly lung exacerbations in high-risk patients, hypertonic saline is relatively inexpensive to produce and administer.

For more information on the use of aerosolized hypertonic saline in cystic fibrosis, please review our Clinical Bulletin on Hypertonic Saline and contact us with any questions you may have. Questions may be directed to Jason Ranville at [iranville@cff.org](mailto:iranville@cff.org) or (301) 841-2617.

Thank you for your attention to this important matter.

Sincerely,

Preston W. Campbell, III, M.D.  
Executive Vice President for Medical Affairs

Bruce C. Marshall, M.D.  
Vice President of Clinical Affairs

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## **CYSTIC FIBROSIS FOUNDATION INFO-POD**

Information You Need to Make Benefits Decisions

### **Issue 1: Hypertonic Saline**

*Summary:* Preserving lung function is a crucial element in the care of the individual with cystic fibrosis (CF). Regular use of inhaled hypertonic saline (HS) can reduce exacerbations of lung disease, decrease time on antibiotics, and help maintain lung function in CF, and is recommended by the CF Foundation for use in individuals with CF who are at least 6 years of age.

### **What is cystic fibrosis?**

Cystic fibrosis (CF) is the most common life-threatening genetic disease in the United States, affecting approximately 30,000 individuals. In the last few decades, improvements in care have increased the median predicted survival age to over 37 years old,(1) but a steady decline in lung function significantly impacts their lives. Half of the young adults living with CF today have lost at least 30% of their lung function, and 16% of adults with CF are disabled.(1)

Lung disease remains the major cause of disability and death in CF.(2)

*Delaying the progression of lung disease is the best way to improve quality and length of life, and is therefore a major focus of care of the individual with CF.*

### **How can lung function be preserved in CF?**

Damage to the lungs of the individual with CF is caused by obstruction of the airways with thick, dehydrated secretions, blocking effective host defenses and providing an ideal environment for the growth of bacteria such as *Pseudomonas aeruginosa*. Clearing the airways of these secretions through chest clapping and other physical methods has long been a bulwark of CF care. Now, new therapeutics such as hypertonic saline (HS) are available to enhance airway clearance and better preserve lung function in the individual with CF.

### **How does hypertonic saline work?**

In a healthy lung, airway cells lined with cilia sweep debris up and out of the lungs. In the CF lung, however, these cilia are ineffective, unable to beat against the thickened mucus containing invading bacteria and the debris of host immune cells

that die in defense of the airway. Aerosolized HS thins the mucus by pulling water out of the cells lining the CF airway. Thinning the mucus allows the cilia to beat more freely and improves their ability to rid the lungs of debris.(3)

Hypertonic saline may also reduce inflammation in the airway. A recent study showed HS decreased levels of IL-8, an inflammation-promoting molecule normally found in high concentration in CF lung secretions.(4) The added benefit of reducing inflammation could be an important element in controlling CF lung damage.

### **What is the evidence for hypertonic saline?**

In 2011, the CF Foundation commissioned a systematic review of the literature to examine the evidence for chronic therapies for CF, including HS. The review identified 2 randomized controlled trials and 4 crossover trials of HS in CF in individuals who were at least 5 years old (Table I).

The two randomized controlled trials compared HS with placebo in a total of 222 patients with CF (5, 6). Both trials found a moderate improvement in lung function with HS. The longer trial, lasting 48 weeks in 164 patients, also found a decrease in pulmonary exacerbations ( $P<0.02$ ) and in number of days with antibiotic use during exacerbations ( $P<0.001$ ) (5). A third, crossover, trial compared HS to placebo in 19 children with CF who still had normal lung function (7). This study did not detect an improvement in lung function, but did find that HS improved lung clearance index, a sensitive measure of mucus obstruction in the lungs.

Three additional crossover trials compared HS with rhDNase in a total of 80 patients (8-10). Two trials (9, 10) demonstrated improvement in lung function in HS-treated patients over baseline. (The third trial (8) did not show a significant difference in lung function with either HS or rhDNase over baseline, but this trial was reported in abstract form only and was not available for full analysis.)

A Cochrane review on the use of HS in CF (11) recommended the use of HS in individuals with CF, noting an improvement in quality of life and a reduction in pulmonary exacerbations.

After examining the results of the systematic literature review, as well as the Cochrane review, the CF Foundation's Pulmonary Therapies Committee, comprising more than a dozen leading pulmonologists and other CF experts from across the

United States, concluded that HS is safe and generally well-tolerated, especially if preceded by treatment with an inhaled bronchodilator.(12) The most common side effect was cough or bronchospasm, clinically significant in only a few patients. Using the U.S. Preventive Services Task Force grading scheme,(13) the committee found that HS provided a moderate net benefit and recommended its use in patients 6 years and older.(12)

In an effort to extend the benefits of HS to infants and young children, who may profit even more from efforts to preserve lung function, safety trials have recently been conducted in this young population (Table II). These trials, involving a total of 42 infants and young children (4 months to 7 years of age), showed HS was safe and well-tolerated in most patients in this group. While additional studies of hypertonic saline in infants and young children are on-going, it is reasonable to believe that the use of hypertonic saline in this population is safe and will help them maintain lung function in the long-term.

### Is hypertonic saline cost-effective?

Studies have demonstrated that HS improves lung function and quality of life. HS also reduces health care costs:

- The longest-running controlled trial of HS (48 weeks) showed a decrease in antibiotic use from an average of 50 days in patients receiving normal saline to just 11 days in patients receiving HS (5).
- A 3-year retrospective study in 424 people with CF showed that use of hypertonic saline significantly reduced pulmonary exacerbations in patients (14). Pulmonary exacerbations in CF contribute up to 47% of the overall cost of CF care (15).

**Conclusion.** Hypertonic saline preserves lung function and reduces antibiotic usage and hospitalizations, and is thus a cost-effective approach to improving both quality and length of life in individuals with cystic fibrosis.

**Table I. Randomized, controlled trials of hypertonic saline in cystic fibrosis.**

<b>Trial type</b>	<b>Sub-jects (n)</b>	<b>Study Drug</b>	<b>Length of Treatment</b>	<b>Results</b>
Double-blind, randomized, placebo-controlled Elkins et al. (5)	164	7% saline (HS) vs. 0.9% saline (placebo)	twice a day for 48 weeks	<u>Lung function increased (HS vs. placebo) (mL* (95% CI)</u> FVC: +82 mL (12-153) FEV1: +68 mL (3-132) FEF <sub>25-75</sub> : +32 mL (-67-146) <u>Exacerbations reduced (HS vs. placebo)</u> 56% (P<0.02) <u>Antibiotic-days for exacerbations reduced (HS vs. placebo)</u> 78% (P<0.001)
Randomized, open-label Eng et al. (6)	58	6% saline (HS) vs. 0.9% saline	twice a day for 2 weeks	<u>Lung function increased (HS vs. placebo) (95% CI)</u> FEV1%: +15.0(+/-16.0)% vs. +2.8(+/-13)%
Double-blind, randomized, crossover Amin et al. (7)	19	7% saline (HS) vs. 0.9% saline (placebo)	twice a day for 4 weeks	<u>Lung clearance index increased (HS vs. placebo)</u> 2.05 (HS) vs. 1.16 (placebo); (p=0.016)
Randomized, open-label (crossover with DNase) Ballmann et al. (9)	14	5.85% saline (HS)	twice a day for 3 weeks	<u>Lung function increased (HS vs. baseline)</u> FEV1%: +7.7% (p<0.05)
Randomized, open-label (crossover with DNase) Suri et al. (10)	48	7% saline (HS)	twice a day for 12 weeks	<u>Lung function increased (HS vs. baseline) (mean (SD))</u> FEV1%: 3 (21)%

NOTE: A crossover trial (8) comparing HS with DNase, reported in abstract form only, was not available for full analysis.

\*averaged across all measurements taken after start of treatment

**Table II. Trials of hypertonic saline in young children with cystic fibrosis.**

Trial type	Subjects (n)	Study Drug	Length of treatment	Results
Single-dose, open-label Subbarao et al. (16)	13 (infants, 25-140 wks)	7% saline	One dose	No change in respiration, heart rate, oxygen saturation, FEV <sub>0.5</sub> , FEF(25-75) 3 infants coughed during inhalation
Single-dose, open-label Dellon et al. (17)	29 (14 infants, 4mo-3yr; 15 pre-schoolers, 4-7yr)	3% saline OR 7% saline	One dose	No change in vital signs. One pre-schooler had a significant transient drop in FEV <sub>1</sub> after 7% saline. Pre-schoolers had more cough post-treatment in both groups

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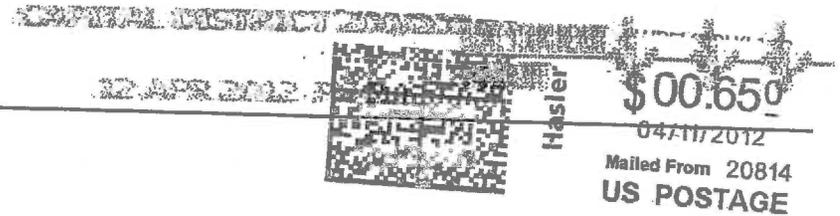
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