DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

AUG 22 2002

TRANSMITTED BY FACSIMILE

Leigh Vaughn, Pharm.D.
Senior Director
Biovail Pharmaceuticals
3725 Concorde Pkwy STE 1500
Chantilly, VA 20151

RE: NDA #50-685
Cedax® (ceftibuten)
MACMIS ID #10744

Dear Dr. Vaughn:

This letter concerns the dissemination of promotional materials for Cedax (ceftibuten). As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed a visual aid (CED241A0102) submitted under cover of Form FDA 2253 by Biovail Pharmaceuticals (Biovail). The visual aid promotes Cedax in violation of the Federal, Food, Drug, and Cosmetic Act and applicable regulations because it makes unsubstantiated efficacy claims about the drug.

The visual aid, entitled "THE RESPIRATORY SYSTEM," includes graphic depictions of various structures of the respiratory system, including the paranasal sinuses, larynx, bronchopulmonary segments, and intrapulmonary airways. The product logo for Cedax and the tag line "Hard to resist" are displayed prominently at the bottom of the visual aid.

Specifically, DDMAC has the following objections:

Unsubstantiated Efficacy Claims

The visual aid suggests efficacy claims that are not supported by substantial evidence, thereby overstating the efficacy of Cedax. Specifically, the tag line "Hard to resist" suggests that it will be difficult for specific microorganisms that infect the respiratory system to achieve resistance against Cedax. Additionally, the tag line suggests that Cedax is effective against drug-resistant pathogens. There is not, however, substantial evidence that supports such resistance claims. Furthermore, there is no evidence to suggest that resistance patterns for Cedax involve mechanisms other than those common to other cephalosporins. To suggest that treatment with Cedax will be less likely to select for drug-resistant pathogens is misleading and may promote inappropriate physician prescribing of Cedax for these pathogens.

The development of resistance to antibiotics is an increasing public health problem. As more and more pathogens become resistant to antibiotics, infections caused by those pathogens become more difficult

to treat. Furthermore, inappropriate prescribing and overprescribing of antibiotics for upper respiratory infections are factors that contribute to the development of resistant pathogens, which pose a significant public health concern.

Requested Action

We request Biovail to immediately cease dissemination of the visual aid (CED241A0102) and any other promotional materials that contain the same or similar claims or representations. In addition, we request that you submit a written response by September 5, 2002, describing your intent and plans to comply with the above. The response should include a list of materials discontinued and the date they were discontinued.

You should direct your response to Dr. James R. Rogers by facsimile at (301) 594-6771, or in writing to the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42 Room 8B-45, 5600 Fishers Lane, Rockville MD 20857. DDMAC reminds you that only written communications are considered official. In all future correspondence regarding this particular matter, please refer to MACMIS ID #10744 in addition to the NDA number.

Sincerely,

{See appended electronic signature page}

Cheryl D. Cropp, Pharm.D., BCPS
James R. Rogers, Pharm.D.
Regulatory Review Officers
Division of Drug Marketing,
Advertising, and Communications

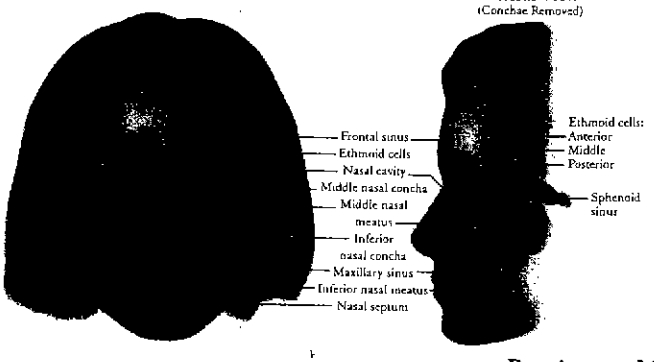
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

James Rogers
8/22/02 02:35:00 PM

THE RESPIRATORY SYSTEM

Paranasal Sinuses

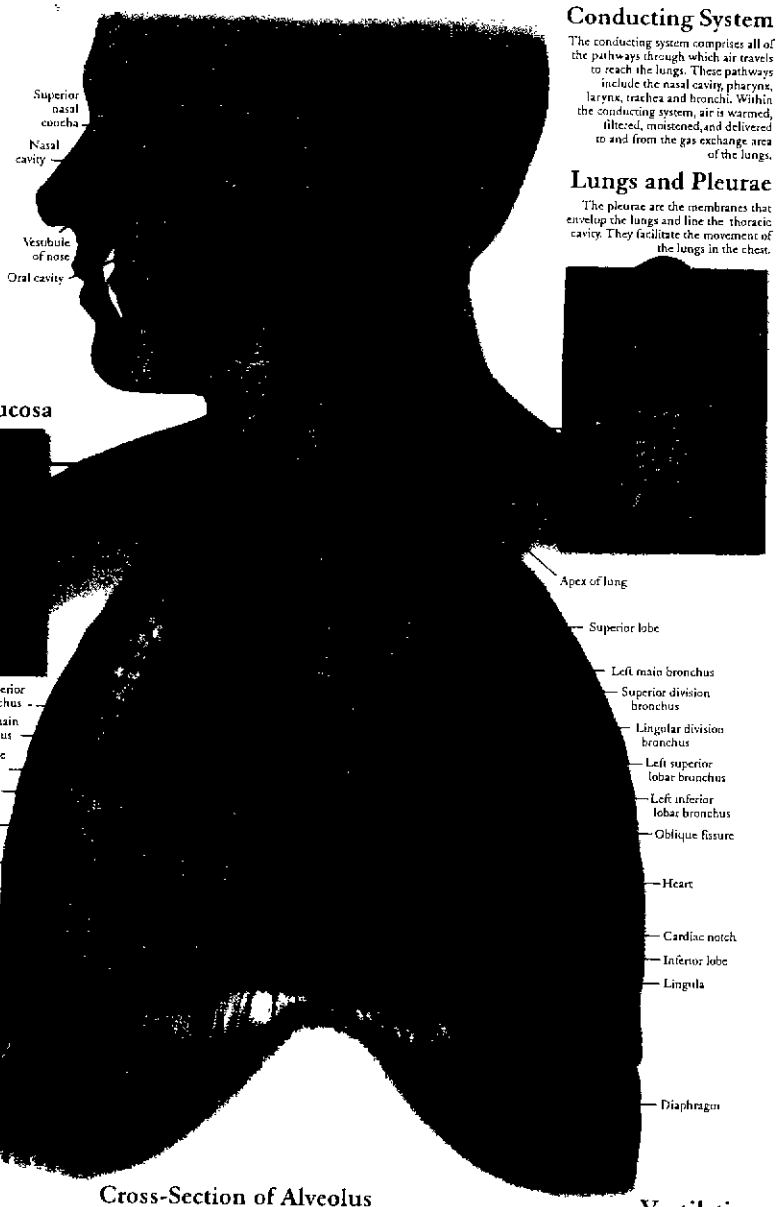


Conducting System

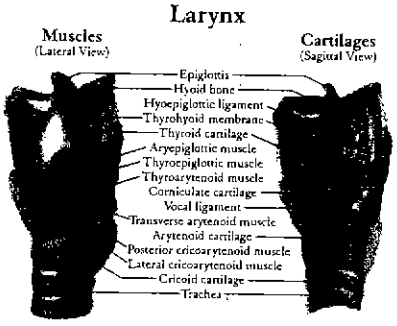
The conducting system comprises all of the pathways through which air travels to reach the lungs. These pathways include the nasal cavity, pharynx, larynx, trachea and bronchi. Within the conducting system, air is warmed, filtered, moistened, and delivered to and from the gas exchange area of the lungs.

Lungs and Pleurae

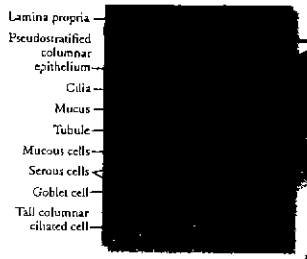
The pleurae are the membranes that envelop the lungs and line the thoracic cavity. They facilitate the movement of the lungs in the chest.



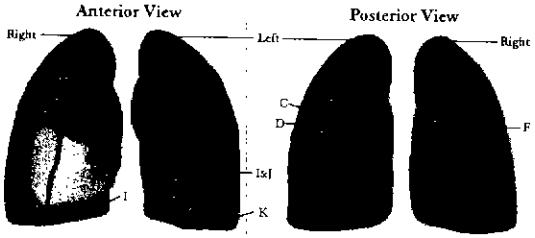
Larynx



Respiratory Mucosa



Bronchopulmonary Segments

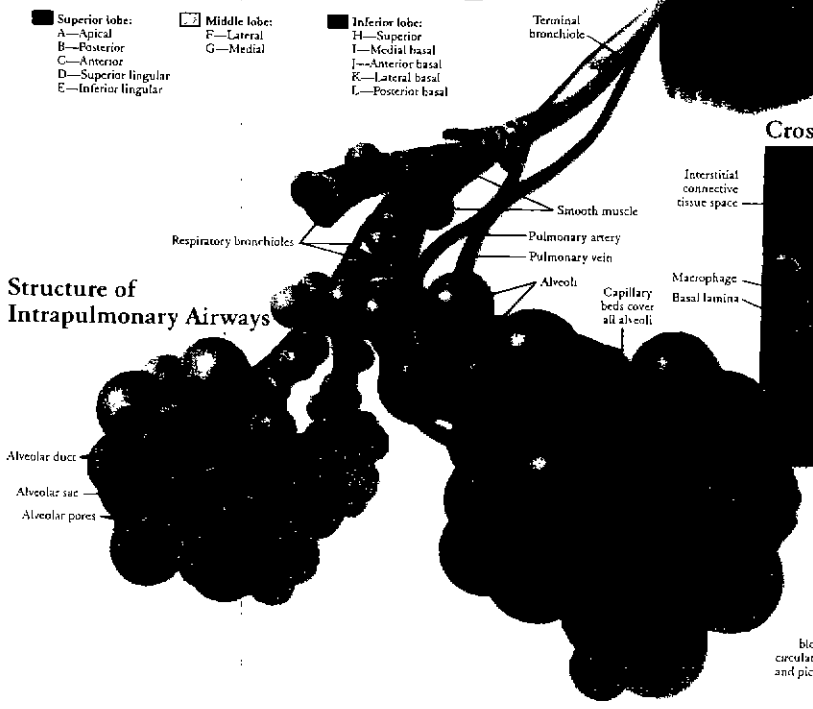


Superior lobe:
A—Apical
B—Posterior
C—Anterior
D—Superior lingular
E—Inferior lingular

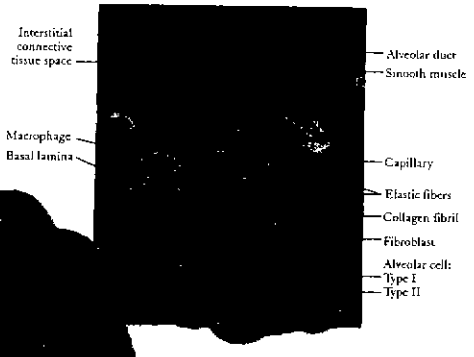
Middle lobe:
F—Lateral
G—Medial

Inferior lobe:
H—Superior
I—Medial basal
J—Anterior basal
K—Lateral basal
L—Posterior basal

Structure of Intrapulmonary Airways



Cross-Section of Alveolus



Ventilation

Breathing, or ventilation, is the movement of air into and out of the respiratory system. During inspiration, the diaphragm and external intercostal muscles contract, causing the rib cage to expand and the volume of the thoracic cavity to increase. Air then rushes in to equalize the pressure. During expiration, the lungs passively recoil as the diaphragm and intercostal muscles relax, pushing air out of the lungs.

Inspiration
Diaphragm contracts (moves down)
Rib cage expands
Lung volume increases

Expiration
Diaphragm relaxes (moves up)
Rib cage retracts
Lung volume decreases

Gas Exchange

The respiratory unit consists of the respiratory bronchiole, alveolar duct, alveolar sac, and alveoli. Gas exchange occurs very rapidly in the millions of tiny, thin-membraned alveoli within the respiratory units. Inside these air sacs, oxygen from air inhaled diffuses into the blood as carbon dioxide diffuses from the blood into the air and is exhaled. Blood then circulates throughout the body, delivering oxygen and picking up carbon dioxide, until returning to the lungs to be oxygenated again.

Medical illustrations by Kimberly A. Martens in consultation with David Yu, M.D.