

Company Tells of Dangers In Overusing Asthma Drugs

By BARRY MEIER A pharmaceutical company has advised Federal regulatory officials of a new report that suggests that excessive use of the most widely prescribed asthma drugs, beta-2 agonists, may increase the risk of fatal asthma attacks.

Officials of the United States subsidiary of Boehringer Ingelheim G.m.B.H. of Germany said in an interview Tuesday that the company recently wrote a confidential letter to the Food and Drug Administration alerting it to the preliminary results of the company-sponsored study in Canada. The study found that asthma patients using twice the recommended daily dosage faced double the risk of a fatal or near-fatal asthma attack. But the report also said that further research was needed to tell whether the increased asthma deaths were caused by the drugs themselves. The drugs are often dispensed in inhalators, with the recommended dosage typically two puffs every four to six hours. Other Side Effects Noted "We don't want people stampeding off the medicine, but they have to be much more alert as to what the side-effects may be," said Dr. Walter O. Spitzer, who directed the recent Canadian study. He is the chairman of the epidemiology and biostatistics department at McGill University in Montreal. He noted that the beta-2 agonists could be life-saving but had to be used very cautiously. Other possible side effects of beta-2 agonists, according to medical studies, include increased blood pressure, irregular or rapid heart beat, difficulty in urination, nervousness and dry mouth.

Faye Peterson, an F.D.A spokeswoman, said agency officials received the Boehringer letter in June but had not acted on it because it does not have the full data from the report, and the initial information was provided to the agency on a confidential basis. She added that the agency was considering a review of beta-2 agonists in light of other recent reports questioning the safety of high doses. Asthma is a lung ailment that causes wheezing and difficulty in breathing and affects 10 million Americans, causing about 4,600 deaths a year. Beta-2 agonists have been used for well over a decade to reduce the effects of asthma attacks, sometimes as the sole treatment. Doctors are now increasingly relying on anti-inflammatory drugs like cromolyn sodium and inhaled steroids and only using beta-2 agonists occasionally to help alleviate asthma symptoms. But because beta-2 agonists provide immediate relief, some patients may overuse them as their symptoms increase. Beta-2 agonists belong to a class of drugs known as bronchodilators that relax and expand lung airways during an asthma attack. One widely prescribed beta-2 agonist is albuterol, which is sold under such brand names as Ventolin and Proventil. The other two beta-2 agonists sold for asthma in the United States are terbutaline, with a brand name of Brethaire, and metaproterenol, sold as Alupent. The recommended dosage on the container of Proventil is two puffs every four to six hours as necessary, but asthma sufferers may be tempted to exceed the recommended dosage when they have trouble breathing. The drug company's letter of warning comes at a time of an unexplained rise in asthma deaths in the United States and elsewhere, as well a recent scientific report from New Zealand that suggested that regular use of beta-2 agonists might be a factor. A recent report by experts assembled by the National Heart, Lung and Blood Institute, a Federal research agency, did not attribute the rise in asthma death rates to any single factor. Some asthma specialists reject any suggestion of a drug link and the new research does not claim to prove one. Physicians also agree that beta-2 agonists are valuable if used with restraint. Experts like Dr. Albert Sheffer, an allergist who teaches at Harvard Medical School, recommend that beta-2 agonists not be used more than once or twice daily. Dr. Spitzer said his study had been submitted to The New England Journal of Medicine. Its results were first disclosed in the July 27 issue of New Scientist, a British magazine. Officials at the F.D.A. and Boehringer declined to release a copy of the company's letter, which was distributed to numerous drug regulatory agencies around the world. But Dr. Spitzer provided a summary of the study's findings and said the company's letters were submitted confidentially to alert regulators, while preserving the research for scientific publication. According to the summary, the study reviewed the health insurance records of 12,300 patients in Saskatchewan treated for asthma from 1978 to 1987. In that period, about 44 individuals died from asthma attacks and another 85 had near fatal attacks that required hospitalization. By looking at patients' prescription records, researchers determined which drugs those 129 individuals had taken and in what quantities and compared that data against drug use in a control group of 600 asthma sufferers. By using statistical measures, researchers concluded that those patients who used two inhalers a month faced a risk of death or near-death that was double that of those patients who used only one a month. One inhaler reflects a month's supply of the drug's recommended daily dose. Dr. Edward Hughes, director of clinical drug safety for the United States subsidiary of the Germany company, Boehringer Ingelheim Pharmaceutical Inc. in Ridgefield, Conn., said the study's findings should be viewed cautiously because those patients taking the greatest amount of the drug might also have the most severe asthma.