Inhaled insulin is approved in Europe and United States

Jeanne Lenzer *New York*

An inhaled form of human insulin, Exubera, has been approved in Europe and the United States for the treatment of type 1 and 2 diabetes in adults. The drug, to be marketed jointly by Pfizer and Sanofi-Aventis, was hailed by the US Food and Drug Administration as the "first new insulin delivery option introduced since the discovery of insulin in the 1920s."

Both the FDA and the European Agency for the Evaluation of Medicinal Products have specified that the drug, which will not be available for several months, is contraindicated in smokers and in patients who have smoked in the preceding six months. It is "not recommended" in patients with asthma, bronchitis, or emphysema.

The European agency has also specified that Exubera is indicated only for "adult patients with type 2 diabetes mellitus not adequately controlled with oral antidiabetic agents and requiring insulin therapy" or for patients with type 1 diabetes who are receiving subcutaneous insulin, "for whom the potential benefits of adding inhaled insulin outweigh the potential safety concerns."

Tests showed that subcutaneous insulin and Exubera reduced haemoglobin A_{1C} to the desired range (<7%) in 23% of patients taking Exubera and in 22% of patients taking subcutaneous insulin.

Steven Galson, director of the FDA's Center for Drug Evaluation and Research, said, "It is our hope that the availability of inhaled insulin will offer patients more options to better control their blood sugars."

Two of the nine members of the FDA's advisory panel on endocrinological and metabolic drugs voted against the approval of Exubera. Critics say Exubera offers no advantage in effectiveness over injected insulin and fails to control postprandial glucose concentrations as well as subcutaneous insulin.

Critics also raised concerns about pulmonary effects and erratic absorption even in patients who were exposed just to secondary tobacco smoke.

FDA briefing documents show that 2 hour postprandial glucose concentrations increased by 1.3 mmol/l in the inhaled insulin group and decreased by 0.5 mmol/l in the subcutaneous group. This, said an FDA medical officer, Karen Mahoney, is a cause for concern, because "postprandial glucose control is increasingly a target of intensive diabetes management, in part because postprandial glucose shows an epidemiologic association with risk of cardiovascular disease."

From next summer some diabetic patients will be using this device to inhale insulin

Some questions about pulmonary effects, which held up approval of the drug for years, remain unanswered. The drug is delivered as a fine powder. Critics say that inhalation of dusts such as coal and cotton has caused a variety of lung diseases.

Sally Seymour, another FDA medical officer, told the panellists that inhaled insulin caused significant increases in the incidence of cough, dyspnoea, sinusitis, and pharyngitis. The drug also caused a 40 ml mean decrease in forced expiratory volume in 1 second (FEV_1), which she said was of small and uncertain clinical significance.

These effects were reversible in type 2 diabetes when the drug was discontinued after 12 weeks, but Dr Seymour said reversal of decreases in FEV_1 among patients with type 1 diabetes was "not convincing" and that it was unknown whether the decreased function would be reversible after longer periods of use. Exubera's label instructs patients to have pulmonary function tests before starting it.

Paul Woolf, acting chairman of the FDA's advisory panel for evaluation of Exubera, voted against approval. He said the drug is great for patients "who absolutely refuse to take shots." But he said that erratic absorption and complex dosing conversions could lead to problems. The drug is packaged in doses of 1 and 3 mg. "How many packets should someone use who needs a 17 unit dose of [human insulin] or, heaven forbid, a 50 unit dose?" he asked. In addition, he said, three blister doses of 1 mg do not deliver the same amount of drug as a single 3 mg dose, making conversions challenging at best. □

Study shows that tobacco firms covertly hired scientists

Roger Dobson *Abergavenny*

The tobacco industry recruited and managed an international network of more than 80 scientific and medical experts in Europe, Asia, and elsewhere in a bid to avoid regulations on secondhand smoke, a new report says.

In one year, 1991, the budget for the programme for Europe alone was $3.3m (£1.9m, €2.8m), say the authors of the report (*European Journal of Public Health* 2006;16;69-77).

The consultants on environmental tobacco smoke, also known as whitecoats, were paid and managed by US lawyers working for the industry, and one of the aims of the programme was to enlist consultants who were prepared to publish research supporting the industry's position that secondhand smoke was not dangerous and that ventilation provided a solution.

"The objective of the program was to influence policy makers, media and the public by providing, through their consultants … information concerning public workplace regulation, indoor air quality and ventilation standards, and scientific claims regarding secondhand smoke," without this information appearing to have been procured by the tobacco industry, says the report.

The consultants carried out these activities by publishing scientific papers and reports, attending conferences, and lobbying. The authors say that the industry's role was not disclosed to the public or was minimised or obscured when it was mentioned.

The report cites a Philip Morris action plan for 1989-92 as an example of what the industry hoped consultants would accomplish: "They should be appropriately encouraged to prepare papers, participate in scientific societies with relevant areas of interest, and take active roles in scientific conferences. Where possible, without compromising a scientist's effectiveness, they should be encouraged to provide statements or testimony for use before government commissions and information to the media."

The authors say the programme began in Europe in 1987, and that by 1989 it included consultants from the United Kingdom, Belgium, Canada, France, Germany, Italy, Finland, and Sweden. It also spread to Asia, and the report says that every member of the organising committee of an international conference on indoor air quality in Bangkok in 1991 was a tobacco industry consultant.

"By 1988 the program included 81 scientists in the major international markets of concern to Philip Morris International. As of early 2004, no document has been located indicating that the program has been terminated," says the report, whose authors, from the University of California, San Francisco, searched tobacco industry documents, including those in the British American Tobacco depository in Guildford, England.

Their study sought to describe how the tobacco industry recruited and managed a secret international network of scientific and medical experts to avoid regulations on secondhand smoke in Europe and Asia.