

DATE: August 25, 2005

TO: Endocrinologic and Metabolic Advisory Committee of the FDA

FROM:

RE: New Drug Application for Exubera

I am writing to express my professional concerns to the FDA's Endocrinologic and Metabolic Advisory Committee as the committee considers providing recommendations to the FDA on inhaled insulin. I am a nurse practitioner and diabetes educator with more than 30 years of experience. I also have type 1 diabetes. The approval of inhaled insulin would provide people with diabetes an alternate tool for the delivery of insulin, and in my role as a diabetes care provider and educator, it will be exciting to have another tool for my patients. There are, however, considerations that should be weighed.

In my practice, I incorporate the American Association of Diabetes Educators' (AADE) 7 Self-Care Behaviors conceptual framework for assessing, intervening, and evaluating my patient's therapeutic and educational needs. The primary focus is anchored in helping patients change behavior for effective diabetes self-management in healthy eating, being active, monitoring, taking medication, problem solving, coping and reducing risks. In this context, we educate people with diabetes to understand the interplay between their diet, exercise, blood glucose monitoring and therapy. The adoption of inhaled insulin will require significant and appropriate counseling/education to facilitate desired behaviors.

I most recently attended an educational session on inhaled insulin presented during the annual meeting of the American Association of Diabetes Educators. On hearing "inhaled," the image of asthma puffers comes to mind. The product being reviewed for approval is different than the delivery mechanisms used to deliver inhaled asthma medication. This is a complex apparatus. It will require significant education from a diabetes educator or other appropriately trained health care provider to help patients to perform the behavior in a proper manner. Used inaccurately or unsafely, this could cause problems for people with diabetes. Storing and cleaning the apparatus is more complex than patients may think. This is a large apparatus and therefore portability needs to be considered.

Central to insulin therapy is careful dose titration. Prescribing nurse practitioners and physicians need to know how to prescribe and titrate the inhaled insulin dose. In a

syringe, one injection is sufficient to deliver the appropriate dose by increments as small as 0.5 units. As I understand the new device, a patient might have to use the inhaler more than once to get an adequate dose and then only in increments of 1 mg (about 3 units). Information shared with the diabetes community to date also leaves unclear how to convert injection doses to inhaled insulin doses.

The diabetes community will also need clear guidance on the target patient for inhaled insulin as patient selection will be key. Among considerations might be whether a patient's baseline health is adequate to inhale an adequate dose and whether measuring lung function should be a screening criteria for patients. The implications for smokers and ex-smokers should also be weighed. In every case, daily blood glucose monitoring will be critical for dosing correctly and to assess if a person's insulin regimen is working and adequate.

As noted above, inhaled insulin will be exciting to people with diabetes. It is very important, however, to help ensure that expectations are realistic. People with diabetes need to understand that insulin injections are still needed for their basal insulin requirements. TV advertising is an example of getting patients interested in blood glucose monitoring that is virtually pain free. In this situation, patients perceive that meters promoted as virtually pain free are a panacea and patients arrive in my office asking for a blood glucose meter that doesn't require blood – something that is not demonstrated in the ads. The reality sets in when the facts are explained.

There are many questions to be answered regarding inhaled insulin: What is the long-term safety profile? How accurate is dosing? Can patients titrate their insulin to their food and exercise? Is the patient's pulmonary health adequate to inhale the insulin? What do patients with acute upper respiratory infections need to do to ensure appropriate dosing? What is the long-term affect on lung tissue? We clearly see the affect on the skin at the site of injection and that triggers questions regarding the affect of insulin on tissue we can't see.

The success of inhaled insulin will rely on ample healthcare provider and patient education to ensure successful and appropriate self-care behaviors of the person with diabetes. The high level of interest in inhaled insulin must be matched with a high level of education. The administration of insulin is just one step required to achieve diabetes control.