

Inhaled insulin: How safe is it?



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The first inhaled insulin (trade name Exubera), was approved in 2006 for use in some people with type 1 and type 2 diabetes in Germany, the USA and other countries. Exubera is a dry insulin powder based on human insulin, and comes with a device for inhaling it. Its effect lasts about as long as the effect of regular human insulin does, but it starts working as quickly as short-acting insulin analogues do.

On 18 October 2007 the manufacturer of Exubera announced that it will stop making this inhaled insulin. Exubera is no longer available. Other manufacturers may produce inhaled insulin in the future. You can read more about insulin analogues in our research summary “Short-acting insulin analogues: Are they better than regular insulin for people with type 2 diabetes?” (URL: <http://www.informedhealthonline.org/index.270.en.html>) , and more about insulin and diabetes in the article “Insulin therapy” (URL: <http://www.informedhealthonline.org/index.264.en.html>) and fact sheet (URL: <http://www.informedhealthonline.org/index.258.en.html>) of the same name.

For most people with diabetes, inhaled insulin would not have fully replaced injections anyway, because Exubera could only be used instead of short-acting insulin. People who also need longer-acting insulin (basal insulin) had to continue injecting it as well as taking the inhaled insulin.

The inhaler device itself is quite a lot bigger than an asthma inhaler. It is about the size of a small drinks can when closed, and extends to about twice that size when in use. The insulin came as a very fine dry powder in blister packs and was available in various doses. A new blister pack of insulin is inserted into the inhaler every time it is used. For higher doses, several blister packs and several inhalations are needed. This is different to insulin injections, where only one injection is usually needed to get the necessary dose. The insulin is inhaled into the lungs in one deep breath through a mouthpiece. It reaches the small air sacs (alveoli) of the lungs and enters the bloodstream there. Most of the insulin, however, stays in the airways and does not get into the blood.

Some parts of the inhaler have to be cleaned regularly and others are replaced every two weeks.

As with any other insulin treatment approach, people using the inhaler have to learn how to take the insulin properly. In this case that means they have to know how much insulin they should inhale and when. They also had training in how to use the inhaler device.

Type 2 diabetes

In January 2006 the regulatory authorities approved inhaled insulin for use in some types of patients. It was not approved for use in children and teenagers, but for the “treatment of adults with type 2 diabetes in whom oral antidiabetics do not work well enough and who need insulin therapy”. But these people can use an insulin pen or syringe instead if they prefer to.

Researchers from the University of Düsseldorf, Germany, and the German Institute for Quality and Efficiency in Health Care (IQWiG) evaluated the available trials on inhaled insulin. They only found one trial, involving about 300 people with type 2 diabetes, that compared Exubera with injected human insulin therapy. This trial did not provide enough data to reliably assess the benefits and harms of inhaled insulin compared with injected insulin. It did not show that inhaled insulin had any additional health benefits compared with injected human insulin in people with type 2 diabetes.

The trials carried out so far were not long enough to be able to assess the effects of inhaled insulin on the development of complications associated with type 2 diabetes.

Type 1 diabetes

Inhaled insulin was also approved for use by “adults with type 1 diabetes in addition to longer-acting injected insulin after careful consideration of the risks and benefits”. So far, however, research has not shown that it enables better blood sugar control in people with type 1 diabetes either. There was no significant difference in HbA1c levels between people who inhaled insulin and those who injected it.

The trials of inhaled insulin in type 1 diabetes are also not able to say how inhaled insulin affects the development of complications associated with this form of diabetes.

Patients' preferences

A further important question is how inhaled insulin compares with insulin injections or pens from the patient's point of view. Only some of the trials published so far provided information about the quality of treatment and quality of life, but they were not carried out in a way that allows a fair comparison. For instance, there are no good trials comparing inhaled insulin with pen systems or pumps. The trials in the analysis probably mainly involved people who injected insulin with syringes. But far more people use insulin pens and pumps rather than syringes in Germany. The data shows that people who used inhaled insulin reported improved quality of life. They were somewhat happier with their treatment than those who used syringes.

Side effects

The trials in the analysis did not allow for a fair comparison in terms of side effects either. This means that the important questions cannot all be answered based on the available data.

Among people with type 1 diabetes, episodes of severe hypoglycemia (low blood sugar) occurred more often in those who inhaled insulin. Also, people who inhaled insulin had higher insulin antibody levels more often than those who injected it. It is not clear what kind of health impact the antibodies could have.

Inhaling insulin has an effect on lung function. In about a quarter of the patients, inhaling insulin caused a mild cough.

The regulatory authorities based their approval of inhaled insulin on trials that only lasted a few months, so they could not include any information on long-term safety. The data available so far, however, suggest that caution should be taken.

It cannot be ruled out that using inhaled insulin over a long period of time may be associated with health risks. Lung function should be checked before the start and after the first six months of treatment. Depending on the outcome, lung function check-ups should be done every year or even after three months already. If the measure of lung function (FEV1) decreases by more than 20 percent, treatment with Exubera should be stopped.

The regulatory authorities have determined that inhaled

insulin is not suitable for the following groups of people:

- people with severe asthma
- people with severe chronic obstructive pulmonary disease (COPD), such as emphysema or chronic bronchitis
- smokers
- ex-smokers who have stopped smoking for less than six months

Inhaled insulin could possibly be very dangerous for smokers because their lungs absorb quite a lot more insulin than non-smokers' lungs do, so they have a bigger risk of severe hypoglycemia.

Inhaled insulin is generally not approved for the treatment of children and teenagers. It is also not approved for use in pregnant women because there has not been enough research in this group. It is not clear whether unborn children are affected by the increase in insulin antibodies observed in people who inhale insulin.

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Note

This health information is a summary of a scientific report published by IQWiG. It is not an assessment of the right to have health care services paid for by statutory health insurance funds in Germany. By law, decisions about paying the costs for diagnostic and therapeutic procedures can only be made by the German Federal Joint Committee (G-BA). The Federal Joint Committee takes IQWiG reports into consideration in its decision-making process. You can find information about the decisions of the German Federal Joint Committee on its English-language website, www.english.g-ba.de (URL: <http://www.english.g-ba.de>).

Glossary

evidence

Evidence is what we call scientific proof from well-conducted, good-quality scientific trials that have been carefully designed to answer specific questions. Depending on the types of questions, different scientific research methods (types of study) are most appropriate to find reliable answers to these questions. Randomized controlled trials (RCTs), for example, are the best way to get reliable evidence on the effectiveness of medical treatments (interventions). This type of study, however, is not the best form of evidence for all possible questions, and does not provide the best answers to all kinds of questions, either. Epidemiological studies, for example, are very suitable for establishing well-founded proof for the spreading of a disease in the population.

asthma

Asthma (asthma bronchiale) is a permanent (chronic) disease with symptoms like coughing and breathlessness often occurring in acute attacks. In asthma, the airways are overly sensitive. The development of asthma is often associated with an overreaction to foreign substances or physical stimuli, frequently in connection with an allergy.

alveoli

The air we breathe in goes through the voice box and then through the windpipe. The windpipe divides into the two main bronchi. Each of these main bronchi branches into smaller bronchi and bronchioles. At the end of the bronchioles, there are groups of tiny air sacs, which are called alveoli or pulmonary vesicles.

emphysema

In emphysema, air is found in a part of the body where it is not supposed to be, or there is an unusual quantity of air in a particular part of the body. One well-known emphysema is pulmonary emphysema. In pulmonary emphysema, the alveoli are destroyed. Air breathed in cannot be fully exchanged, so it builds up in the lungs.

bronchitis

Bronchitis is the inflammation of the airways, also called bronchi. The usual symptom is that phlegm is coughed up almost daily over a longer period of time. Bronchitis can be

acute (temporary) or chronic (permanent).

COPD

In chronic obstructive pulmonary disease (COPD), the airways are permanently narrowed and the lungs are damaged. COPD is not the same as asthma – but both diseases can occur at the same time.

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Sources

Institute for Quality and Efficiency in Health Care (IQWiG). *Inhaled Insulin (Exubera®). Rapid Report A05-22. Version 1.0.* Cologne: IQWiG. April 2006. [Full text (URL: http://www.iqwig.de/download/A05-22_Rapid_Report_Inhaled_Insulin_Exubera.html)].

The German Institute for Quality and Efficiency in Health Care (IQWiG)

The German Institute for Quality and Efficiency in Health Care (IQWiG) was established by legislation to provide evaluations of the effectiveness, quality and efficiency of healthcare services. This includes the assessment of medicines as well as the publication of health information for consumers and patients.

Evidence basis of our health information

Our information is based primarily on systematic reviews of the effects of health care. Systematic reviews are necessary to gain an objective picture of health care. In order to do this, a clear question is formulated. Researchers then find all the relevant studies that could answer this question. They then evaluate those studies.

You can find a list of the evidence and other scientific literature on which this information is based at **www.informedhealthonline.org**

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