Diabetes UK is one of Europe’s largest patient organisations. Our mission is to improve the lives of people with diabetes and to work towards a future without diabetes through care, research and campaigning. With a membership of over 170,000, including over 6,000 health care professionals, Diabetes UK is an active and representative voice of people living with diabetes in the UK.

### Facts about diabetes

- There are 1.8 million people with diabetes in the UK, equivalent to three percent of the population.\(^1\)
- Diabetes is set to increase. It is predicted that diabetes prevalence will double world-wide, rising to at least 5% by 2010, accounting for 3.07 million people in the UK.\(^2\)
- Diabetes affects the young and old, and has particularly poor outcomes in those of lower socio-economic status and in those from black and minority ethnic groups.\(^3,4\)
- Evidence is available supporting the need for improved education of people with diabetes and their carers if better control and improved outcomes are to be achieved.\(^5,6,7\)
- Diabetes, if undetected or not well managed, can lead to many complications and have a devastating impact on quality of life.

### Executive Summary

Diabetes UK believes that people with diabetes should have equal access to the best diabetes care and health outcomes available on the basis of need and appropriateness. Commitment to a modern and responsive health service requires that healthcare professionals are able to prescribe effective treatments to meet the individual needs and choices of those with diabetes. In order to reduce the impact of diabetes on the individual, their carers and the NHS, people should, in consultation with their healthcare team, be able to choose the treatment that gives them the best control of their diabetes and the best quality of life. Diabetes is about self management\(^8\). People
living with the condition need to tailor the advice and information provided by healthcare professionals with the tools and treatments available to achieve a level of control which allows them the best quality of life. Good control of diabetes has been shown to delay and prevent the long-term complications of the condition.\textsuperscript{9,10,11}

**Background**

Diabetes develops when the body can no longer produce its own insulin (Type 1) or when the body can still make some insulin though not enough for its needs or when the insulin that the body does make is not used properly (Type 2) and insulin resistance occurs. Type 1 diabetes is the type that is most common in people under the age of 30. Type 2 diabetes usually appears in people over the age of 40, although there is evidence that it is appearing in younger age groups. Type 1 diabetes requires insulin treatment, together with a balanced diet and appropriate levels of physical activity. Type 2 diabetes is initially treated by diet alone, then by diet and tablets, then using multiple tablet therapy and, finally, by transfer to insulin injections (with or without tablets in addition).\textsuperscript{12}

The main aims of treatment are to achieve near normal blood glucose levels and tackle associated cardiovascular risk factors which, together with a healthy lifestyle, will help to improve well being and protect against long term damage to the eyes, kidneys, nerves, heart and major arteries. The goal of treatment should therefore be for people with diabetes to achieve an HbA1c level of less than 7.0 per cent or as close to normal as possible while at the same time minimising their risk of hypoglycaemia\textsuperscript{13,14,15}. The role of the individual with diabetes in managing their condition is vital.\textsuperscript{16} Although clinicians advise on therapy and treatment, it is the individual who has to interpret that information and use it on a day–to-day basis, in order to achieve their ideal balance between quality of life now and reducing the risk of short and long term complications.

**Management**

In practice, there are several insulin regimens used in order to try and maintain good blood glucose control. Which regimen is chosen depends upon many factors, including the age of the person with diabetes, their ability to self inject, and the level of blood glucose control they are trying to achieve. The most common regimen is twice daily injections, combining short and
medium acting insulins. However, some people with diabetes find these injections a major problem. Compliance is a major factor that influences good control, with many reporting that non-compliance in those on insulin can be quite high.\textsuperscript{17} Although essential, injections interfere with daily activities and can lead to patients developing needle phobia.\textsuperscript{18, 19} Insulin injections have evolved and now self-injection pens are available. These are easier to use and deliver an accurate dose of insulin but they do not remove the need for regular injections.

The concept of delivering insulin directly to the lungs (pulmonary insulin) aims to reduce daily injections and may be beneficial for those with needle phobias. The principle underlying inhaled insulin is that the large surface area of the lung enables the relatively large insulin molecules to cross from the alveolar epithelial walls by transcytosis. It is then released and taken up by endothelial cells to be ultimately released into the pulmonary capillaries, and thence into the bloodstream. After inhalation, a relatively small amount of the dose inhaled (approximately 15\%) is available for absorption, but given a sufficient inhaled dose, this is clinically effective.\textsuperscript{20, 21} The onset of action is more rapid than soluble insulin\textsuperscript{22} and similar those of analogue insulin after subcutaneous injections, with a duration of action which is between analogue and soluble insulin\textsuperscript{23}.

Clinical trials suggest pulmonary delivery of insulin is encouraging. These trials suggest that inhaled insulin may be as effective as injected insulin and superior to oral agents in lowering blood glucose in patients with diabetes.\textsuperscript{24} For example, a phase III study involving 328 patients with type 1 diabetes showed that patients using inhaled insulin before meals plus two daily insulin injections had glycaemic control comparable to patients on four insulin injections. Compared with patients who received only insulin injections, patients receiving inhaled insulin experienced significant reductions in both fasting plasma glucose levels (blood glucose measured before breakfast) and two-hour post-prandial glucose levels (blood glucose measured after meals).

In studies comparing inhaled and injected insulin, pulmonary function is similar in for both modes of insulin treatment in Type 2 diabetes, and is also similar in Type 1 with the exception that reduced carbon monoxide diffusing capacity following inhaled insulin treatment.\textsuperscript{25} The significance of this reduction is unclear, and might be of concern if it continues to decline with
prolonged treatment. However these studies are short term (6 months) and any long-term effects of inhaled insulin are as yet unknown. Inhaled insulin is effective. Improvement in glycaemic control seen during 6 months treatment of inhaled insulin in both Type 1 and 2 diabetes is comparable with that seen using sub-cutaneous injections.\textsuperscript{26} There is a very small reduction in the frequency of hypoglycaemia events with inhaled insulin, but this is unlikely to be of clinical significance.\textsuperscript{27} Insulin antibodies titre rise following initiation of inhaled insulin, but this is not associated with any adverse clinical outcome.\textsuperscript{28}

While inhaled insulin appears efficacious, concerns have been raised about the safety of inhaled preparations and whether it will compromise lung capacity or damage lung tissue in long-term use. Inhaled insulin produces cough in a significant minority of people (approximately 20%), but this reduces with frequency and intensity with time.\textsuperscript{29} Additional studies are being conducted to address this safety concern and determine the long-term pulmonary safety profile of inhaled insulin. In addition, it is important to make sure that patients who are exclusively managed with inhaled insulin can get access to an inhaler wherever they are in the world. If an inhaler broke and the patient could not get access to a replacement, there would be potentially fatal repercussions.

**The inhaled insulin device**

The use of the inhaled insulin device will require some training as there are 5 steps to insulin administration. The insulin delivery device is extended by pulling down a ring pull at the base to extend the chamber. The dried insulin is inserted using a blister pack which will contain either 1 or 3mg of insulin with manitol, glycine and citrate. The device is pressurized using the handgrip. The blister package containing insulin is punctured and insulin is aerosolized into the holding chamber by the transjector. Insulin administration occurs by taking a single large breath through the chamber, held for about 10 seconds. If further doses of insulin are required, the process must be repeated. The costs of manufacturing and maintaining the device are significant, although the amount this will cost the NHS is unclear at present. Healthcare professionals need to be taught how to use the inhaler and pass this knowledge on to patients. Time and funding must be allocated to allow healthcare professionals to adequately complete this training.
Views of people with diabetes

Diabetes UK provides a telephone helpline service which takes over 50,000 enquiries a year. Although the information gained from the Diabetes UK Careline is qualitative, it does reflect the concerns and interests of many people with diabetes. In August 2005, Careline carried out some questionnaires with people with diabetes to obtain their views on inhaled insulin. We wanted to find out what people with diabetes felt were the problems with injecting insulin, what the perceived potential advantages and disadvantages of inhaled insulin and whether or not they might want to switch to it, if the opportunity arose.

Results

26 people with diabetes were interviewed over the phone after calling Careline with an enquiry. (Please see Appendix 1 for the questionnaire format). 20 of the respondents already used insulin injections and 6 did not. We asked the respondents about the kind of problems they experienced with insulin injections, if any. The chart below shows these responses.

We then asked the respondents if they would consider using inhaled insulin, if it was available. It can be seen from the chart that just over three quarters would consider using it.
Respondents said they would feel less self-conscious using an inhaler rather than an injection in public and the reduction in injections would be most welcome. Many thought it would be easier to administer than injections and were keen to give the new treatment a try. However, concerns were expressed about the size of the inhaler needed and thought that this might take away some of the benefits. It was thought that the inhaler might be too big so it would be hard to transport and that it might in fact draw more attention to the user. We asked respondents in a later question what potential disadvantages there might be to inhaled insulin and again the size issue was raised. Respondents also thought that there might be trouble with accurate dosing and that we are as yet unclear what the long-term effects of inhaled insulin might be on the lungs. Nonetheless, the general feeling was that it would be an advantage to not have to do so many injections. People felt that the bruising, having to deal with needles in public and finding sites to inject in, among other things, all adversely affected their lives and some change in this would be of benefit. It is telling that most people who were previously treated with subcutaneous insulin and even those on tablets treatment opt to continue on inhaled insulin.

Who might benefit, and who will get inhaled insulin?

If there were no cost, safety of efficacy constraints, one could envisage that most people with insulin treated diabetes might like to be offered the choice of bolus inhaled insulin with their basal insulin. This opportunity is unlikely to be possible as it is probable that inhaled insulin therapy will carry a significant premium in cost. Clinicians will be able to immediately identify a
core of patients, typically with Type 1 diabetes, who have either poor glycaemic control and would benefit from multiple daily insulin administration, but do not want more frequent insulin injections because of inconvenience or needle phobia. It is likely that such people will be the earliest to be transferred over to inhaled insulin. Similarly, people who are on multiple daily insulin injection, but who have problems with lipohypertrophy or hardening of injection sites, and some with Type 2 diabetes who have similar issues, may benefit from inhaled insulin. But what about people with Type 2 diabetes, who have reached the end of effective tablet treatment? Should inhaled insulin be the treatment of choice for those who are now started on once daily lisophane or long-acting insulin analogue or twice daily mixed insulin regimens? Many diabetologists would say no, but if the patient choice outlined in the NSF for diabetes means anything at all, this therapeutic option will have explained and offered. For those people who decline insulin injection, inhaled insulin may be a useful tool.

A further issue will be people who will not be suitable for inhaled insulin. Smokers and recent ex-smokers, people with significant lung disease and women who may become pregnant are likely to be excluded. But there are questions around how to assess whether patients who say that they are non-smokers really are, and how severe lung disease needs to be? Will a “bit of asthma” be exclusion? It will not be practical to do pulmonary function test of sufficient sophistication in either general practice or most diabetic clinics.

**Conclusion**

Inhaled insulin offers a novel and interesting new mode of treatment for people with diabetes and it is likely that there will be enormous demand for it if it becomes available. Although we recognise the need to balance increased cost for treatments against health and quality of life benefits, Diabetes UK feels that all people with diabetes should have choice in the method of their treatment, in consultation with their healthcare professionals. Living with diabetes is about self-management. When people have a choice of therapies and are involved in decision-making, they feel that they are more empowered to take control over their condition. This often helps motivate them to take better care of themselves. The views of patients need to be considered as their qualitative experience is valid. Inhaled insulin provides more flexibility in treatment regimes. This would help many people with diabetes to improve their own quality of their life and might help improve compliance.
Appendix 1

Inhaled Insulin Survey

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<th>Gender</th>
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<td>Age</td>
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<tr>
<td>Type</td>
<td>1</td>
<td>2</td>
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<tr>
<td>Length of diabetes</td>
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<tr>
<td>Do you use insulin injections</td>
<td>Y</td>
<td>N</td>
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1. How has having diabetes affected your lifestyle (e.g. insulin injections/diet/hospital visits)?

________________________________________________________________________
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2. What problems do you experience with insulin injections if any?

<table>
<thead>
<tr>
<th>Frequency of injections</th>
<th>Injecting in public</th>
<th>Problems with locating sites</th>
<th>Fear of needles</th>
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<table>
<thead>
<tr>
<th>Pain</th>
<th>Other (please state)</th>
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3. Would you consider using inhaled insulin? Y N (please explain)

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4. What would you see as the potential advantages/disadvantages of using inhaled insulin?

________________________________________________________________________
24 Skyler JS, Piper E. Efficacy and safety of an intensive inhaled insulin regimen in patients with Type 1 diabetes. PLEASE NOTE THIS WAS SPONSORED BY SANOFI AVENTIS
30 Rosenstock J, Cappelleri J.C, Bolinder B, and Gerber R.A, Patient Satisfaction and Glycemic Control After 1 Year With Inhaled Insulin (Exubera) in Patients With Type 1 or Type 2 Diabetes. Diabetes Care 27: 1318-1323.