

**Important:** Example only. Content is general information and not medical advice. Not for use in making clinical decisions.

What are the positives and negatives surrounding the use of Inhaled Insulin?

Positives	Negatives
<ul style="list-style-type: none"> <li>(HE) Potential for improved blood glucose control in type 2 diabetes</li> </ul> <p>Sources: Pfizer EXUBERA product insert, <a href="http://www.pfizer.com/pfizer/download/uspi_exubera.pdf">http://www.pfizer.com/pfizer/download/uspi_exubera.pdf</a>            FDA Endocrinology Review Document (2005) <a href="http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4169T1.pdf">http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4169T1.pdf</a></p>	<ul style="list-style-type: none"> <li>(C) Does not necessarily eliminate injections. Certain individuals with type 2 diabetes <i>may</i> require basal insulin; basal insulin <i>is required</i> for everyone with type 1 diabetes.</li> </ul> <p>Source: Pfizer</p> <ul style="list-style-type: none"> <li>(HE) Common side effects from inhalation—e.g., cough, chest discomfort, dry mouth.</li> </ul> <p>Sources: Pfizer; 7 November 2006, Annals of Internal Medicine, Volume 145, Number 9, p 670. <a href="http://www.annals.org">http://www.annals.org</a></p> <ul style="list-style-type: none"> <li>(HE) Clinical trials indicate lung function reduction using pulmonary function tests in both type 1 and type 2 diabetes. Lung tests are required prior to starting inhaled insulin therapy; 6 months thereafter; annually thereafter. More frequent tests may be required in certain situations.</li> </ul> <p>Source: Pfizer EXUBERA product insert</p> <ul style="list-style-type: none"> <li>(C) Large, obtrusive delivery device—about the size of a tennis ball container when open.</li> <li>(C) Requires repeated pumping by user before insulin can be inhaled.</li> </ul> <p>Source: <i>Pfizer's Inhaled-Insulin Diabetes Drug Falters in Domestic Sales</i>; The Tech (MIT), April 10, 2007, p3.  <i>This device is large and will attract attention in public. Patient compliance might be a problem for some users.</i></p> <ul style="list-style-type: none"> <li>(HE) Only 10 ~ 15% of the insulin released through the inhaler is absorbed into the bloodstream. Where does the 85 ~ 90% go that was not absorbed? Long-term effects?</li> </ul>

Category Abbreviations:

- Health Effects (HE)
- Convenience (C)
- Personal Value (PV)

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	<ul style="list-style-type: none"> <li>• (HE) “In clinical studies...increases in insulin antibody levels...were significantly greater for patients who received EXUBERA than for patients who received subcutaneous insulin only. No clinical consequences of these antibodies were identified <u>over the time period</u> of clinical studies...however, the long-term clinical significance of this increase in antibody formation is <u>unknown</u>” Source: Pfizer EXUBERA product insert.</li>   <li>• (HE) Previous drive to reduce increased insulin antibody formation in patients using subcutaneous insulin because of concerns they could delay and render unpredictable insulin absorption or have immunologic consequences. Past concerns that antibody antigen complexes may increase risk of microvascular disease. Sources: BMJ 2004;328:1215-1216 (22 May), doi:10.1136/bmj.328.7450.1215 <a href="http://www.bmj.com/cgi/content/full/328/7450/1215">http://www.bmj.com/cgi/content/full/328/7450/1215</a> FDA Endocrinology Review Document (2005) <a href="http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4169T1.pdf">http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4169T1.pdf</a> Exubera Drug Monograph, July 2006, Table 16, Postmarketing Clinical Trial Requirements <a href="http://www.pbm.va.gov">http://www.pbm.va.gov</a>; Monograph link: <a href="http://www.pbm.va.gov/monograph/Inhaled_Insulin_Monograph.pdf">http://www.pbm.va.gov/monograph/Inhaled_Insulin_Monograph.pdf</a> <i>Note: What are the long-term risks of higher insulin antibody levels associated with inhaled insulin? Consequences?</i></li>   <li>• (HE) Concerns regarding <i>pulmonary toxicity</i> due to the immunogenic and growth-promotion properties of insulin. Source: 7 November 2006, Annals of Internal Medicine, Volume 145, Number 9, pp 673-674. <a href="http://www.annals.org">http://www.annals.org</a></li>   <li>• (HE) Are there any implications of using this delivery method during a cold, bad chest cold, or other viruses, e.g., increased alveoli or other lung structure stress; reduced or increased insulin absorption? (C) Must one replace inhaled insulin delivery with injection delivery during illness?</li> </ul>

Positives	Negatives
	<ul style="list-style-type: none"> <li>• (HE) Contraindicated for people with lung diseases such as asthma and COPD; no smoking for 6 months prior to beginning use of inhaled insulin and no smoking thereafter. (Could cause unpredictable and increased or decreased insulin bioavailability, resulting in increased risk of hypoglycemia or hyperglycemia.) Source: Pfizer EXUBERA product insert.</li> <li>• (C) Complex and confusing dosing schemes. For example, three 1 mg blisters <b>ARE NOT EQUAL</b> to one 3 mg blister.</li> <li>• (PV) Does <i>not</i> permit fine adjustment of insulin dosages. Dosages of 0.5 unit, 1 unit, or 2 units are not possible. Source: Pfizer EXUBERA product insert.</li> <li>• (HE) Pfizer post-marketing agreement with FDA (U.S. Food and Drug Administration) for approval. Tests began July 2006; final report due to FDA December 2015.             <ol style="list-style-type: none"> <li>1. Estimate the relative risk of greater than a 20% decline in lung function using pulmonary function tests.</li> <li>2. Clinical risk with insulin antibody formation and relative risk of developing allergic and immune disorders.</li> </ol>             Source: <a href="http://www.pbm.va.gov">www.pbm.va.gov</a>; Monograph link: <a href="http://www.pbm.va.gov/monograph/Inhaled%20Insulin/Monograph.pdf">http://www.pbm.va.gov/monograph/Inhaled Insulin, Monograph.pdf</a>; Section: <i>Postmarketing Study Commitments</i>;           </li> </ul>