

ARTICLE

Insulin delivered with inhaler

– the case strengthens



ICONOVO



There is a growing interest in delivering drugs with inhalers. Not only drugs that work in the airways – such as those against asthma and chronic obstructive pulmonary disease (COPD), but also drugs that acts systemically.

This is because many drugs are easily and rapidly taken up from the outside of the mucosa in our lungs, to our blood. Like

oxygen. This happens much faster than drug uptake from the digestive system, or after a subcutaneous injection. After inhalation, a drug enters the bloodstream almost as fast as after an intravenous injection.

Inhalers are thus an interesting option for the delivery of insulin to patients suffering from diabetes, that are currently taking subcutaneous

injections. The patients could avoid frequent injections and rather inhale insulin.

After subcutaneous delivery insulin molecules form hexamers, whose dissociation is difficult to predict and regulate. As a result, the uptake is relatively slow, and continues for prolonged periods that are not desirable.

During a period with high blood glucose, the insulin taken by inhalers would in contrast enter the bloodstream without delay. The

effect will be immediate, thus avoiding glucose to potentially damage the small blood vessels. And after the administration, the insulin will not remain in the subcutaneous fat for prolonged periods, thus avoiding risk for unnecessary low blood glucose levels.

It should thus be much easier with inhalers than with injections to adjust and fine-tune doses, to reach a steady glucose level, and avoiding dangerous high and lows in blood glucose levels.

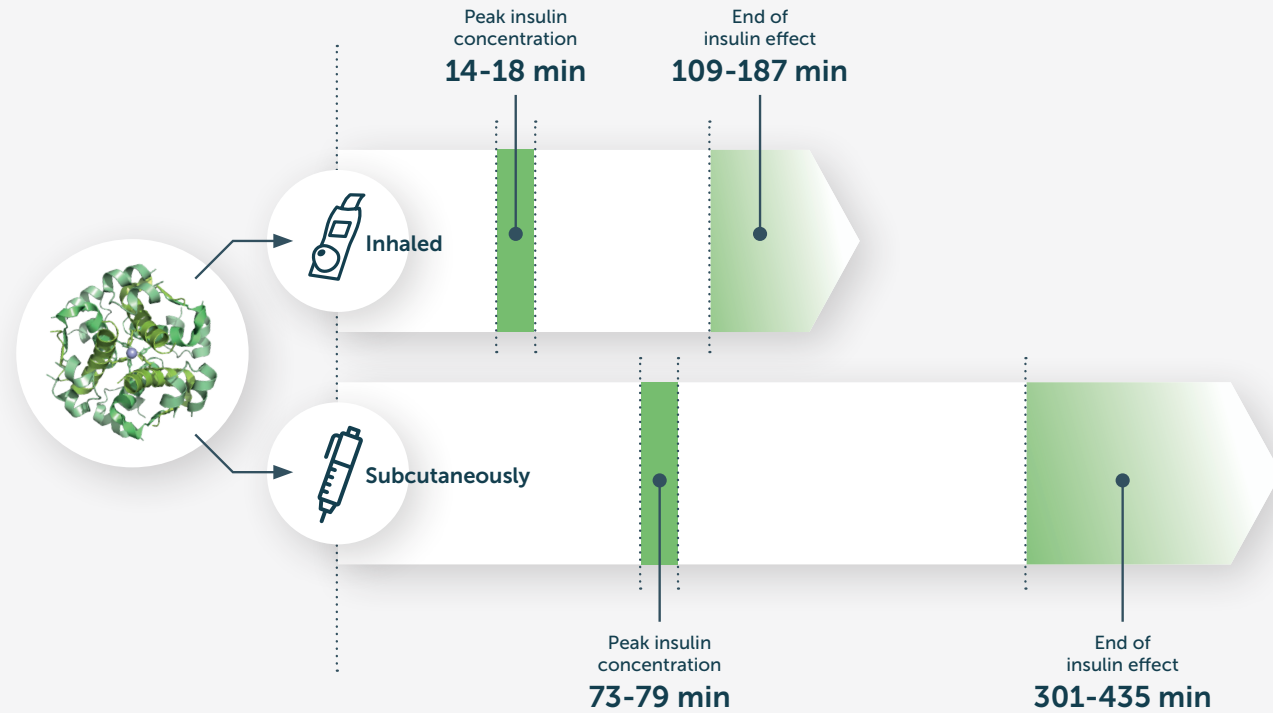


When the first formulations of insulin for inhalation reached the market, FDA demanded post marketing comparisons of response and kinetics between the inhalation formulation and subcutaneous insulin delivery.

Those comparisons were published last autumn in **Clinical Pharmacokinetics** and showed that compared to subcutaneous injections, inhaled insulin had

- faster onset
- shorter duration, and
- a need for higher dose.

More specifically, the study compared an inhaled dry-powder recombinant insulin with a standard subcutaneous injection of insulin lispro, a fast-acting insulin analogue. The so called euglycemic clamp method was used to measure the effect of different doses of insulin and the duration of these effects.



The study showed that inhaled insulin had a faster onset than subcutaneously administered, and a shorter duration. Peak insulin concentration occurred 14-18 minutes after inhalation, compared to 73-79 minutes after subcutaneous injection. And the effect

had vanished 109-187 minutes after inhalation, but not until 301-435 minutes after injection.

Furthermore, the study indicated a weaker effect per unit dosed, caused by a lower bioavailability of the drug through the lung.

This is mainly caused by losses in the upper airways, but to a smaller extent also by breakdown in the lung. Many inhalators doesn't deliver more than 25% to the lung, but by optimizing the choice of inhalator, and formulation of insulin, the losses can be reduced to 50%, thus saving expensive drugs.

The authors of the study conclude, that when changing from injections to inhalation, the dosing must be reconsidered. Both because

of differences in kinetics and in bioavailability.

Inhalation has thus been shown to be a secure and efficient way to deliver insulin, and we now learn more about the details necessary to fully benefit from its advantages.

Delivery through inhalation is a focus area for Iconovo. To learn more about this, and our innovative work in inhalation solutions, please visit [iconovo.com](https://www.iconovo.com).

The logo for Iconovo, featuring the word "ICONOVO" in a bold, white, sans-serif font. The text is centered within a large, orange, rounded shape that tapers to a point on the left and right sides, resembling a stylized arrow or a drop. The background of the entire page is white, with a large, light gray, rounded shape on the right side that mirrors the orange shape on the left.

ICONOVO

ICONOVO AB

Delta 6
Ideongatan 3 A-B
SE-223 70 Lund
SWEDEN

CONTACT

Fredrik Radencrantz
Director Business Development
+46 73-834 11 88
fredrik.radencrantz@iconovo.se