

# Clinical Summary



**For diabetes management, the application of insulin by the InsuJet™ results in a complete administration of medicinal product in the subcutaneous layer. Tolerability, total insulin absorption, total insulin action and total blood glucose lowering effect are equivalent to conventional needle injections.**

Injections by the InsuJet results in a complete administration of medicinal product in the subcutaneous layer and a faster uptake and thus an earlier pharmacologic effect.

Due to the faster absorption of insulin an (semi) endogenous pharmacokinetic insulin profile is created. A low and delayed peak of insulin could lead to hyperglycaemia while eating and to hypoglycaemia shortly after the meal due to remaining high systemic insulin concentration.



## More suitable for the treatment of patients with needle-phobia, or patients who wish to administer insulin without needle

Needle phobia is common, many patients with diabetes perceive insulin injections as painful or experience some form of anxiety with injections(1), the presence of which is strongly associated with nonadherence and poorer glycemic. The absence of the needle in the InsuJet may help in the treatment of patients with needle-phobia. This is supported by Post Market Surveys, where 91% of the users is choosing the InsuJet as a treatment method out of fear for needles.

## More rapid insulin absorption with faster time to maximum insulin concentration and faster offset of action

Subcutaneous (SC) administration of multiple daily insulin injections is effective for achieving tight glycemic control but is associated with some limitations. Current rapid insulin analogs when administered subcutaneously do not replicate the normal pancreatic response and are often associated with immediate postprandial hyperglycaemia and delayed post-meal hypoglycaemia.

This is mainly due to slower onset and offset of action of subcutaneously absorbed insulin. Faster insulin action to mimic endogenous insulin physiology is therefore desired to minimize postprandial glycaemic excursions. Faster insulin action using the InsuJet is reported in various clinical investigations of the InsuJet (2,3).



## Reduce obesity dependent insulin absorption variability

For achieving tight glycemic control (especially postprandial), it is important that insulin absorption is stable, and does not depend on factors such as patient obesity.

Obesity has been reported to be associated with delayed insulin absorption(4). Injection with the InsuJet does not result in obesity dependent absorption variability as observed with needle injections(5).

## Reduce the risk of needle stick injuries and cross contamination

The use of the InsuJet™ reduces the risk of needle-stick injuries and cross contamination for patients and health care providers.

The absence of needle sharp that can impose biological hazards to the patient, caregivers, healthcare providers and others in the direct environment or involved in the disposal of the contaminated needles is a meaningful benefit.

## Reduce the risk of intramuscular injections

The InsuJet targets the subcutaneous tissue just below the dermis reducing the chance of intramuscular injection. Patients wish to avoid intramuscular injections, as they considerably increase the variability of insulin absorption and may impair glycemic control in insulin-dependent diabetic patients(6). For conventional insulin therapy, accidental intramuscular (IM) injections are very common, and can be caused by incorrect injection technique, low fat percentage and incorrect needle length.





# Improved early postprandial glucose control

The overview summarizes the various clinical investigations conducted with the InsuJet device, both on healthy volunteers as well as diabetic patients, to support the above clinical claims.

Links to the studies are provided, and the studies have been published in credible journals, meaning that they have been peer reviewed.



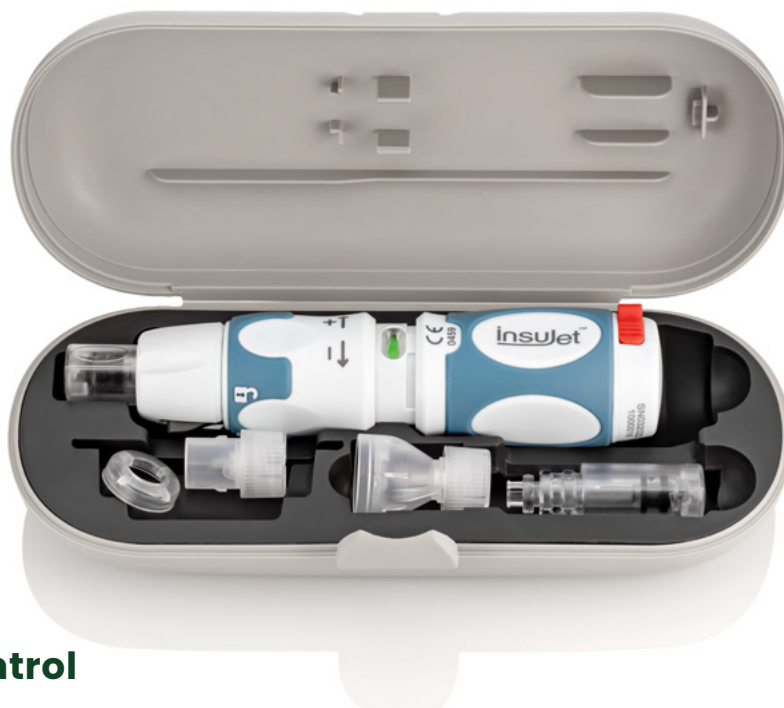
## Insulin administered by needle-free jet injection corrects marked hyper-glycaemia faster in overweight or obese patients with diabetes

Adult, overweight or obese (BMI  $\geq 25$  and  $\leq 40$  kg/m<sup>2</sup>) patients with type 1 diabetes (n=10) or insulin-treated type 2 diabetes (n=10) were enrolled in a randomized, controlled, crossover study. On two separate occasions, patients were instructed to reduce insulin dose(s) to achieve marked hyperglycaemia (18–23 mmol/l). Subsequently, insulin aspart was administered either by jet injection or by conventional pen, in a dose based on estimated individual insulin sensitivity. Pharmacodynamic and pharmacokinetic profiles were derived from plasma glucose and insulin levels, measured for 6h after injection.

It was concluded that administration of rapid-acting insulin by jet injection results in faster correction of marked hyperglycaemia in overweight or obese patients with insulinrequiring diabetes.

The studies show that the application of insulin by the InsuJet results in a complete administration of medicinal product into the subcutaneous layer. The effects on postprandial glucose levels, insulin absorption, tolerability, are similar to better following administration of insulin by InsuJet compared with conventional needle injection. The varies studies also show that many patients would prefer the device if they were asked to choose.





## Glucose Control

Clamp studies have shown that the absorption and action of rapid-acting insulin are faster with injection by a jet injector than with administration by conventional pen. To determine whether these pharmacokinetic changes also exist in patients with diabetes and benefit postprandial glucose control, a comparison was made of the pharmacologic profiles of insulin administration by jet injection versus conventional insulin pen after a standardized meal in patients with type 1 or type 2 diabetes.

Results showed that insulin administration by jet injection resulted in shorter time until peak plasma insulin level and reduced hyperglycemic burden during the first hour compared with conventional administration. Jet injection did not, however, significantly reduce the hyperglycemic burden during the 5-h period thereafter. There was no indication that the jet injector performed differently in patients with type 1 and type 2 diabetes.

It was concluded that the considerably more rapid insulin absorption after administration by jet injector translated to a significant if modest decrease in postprandial hyperglycemia in patients with type 1 and type 2 diabetes. The improved early postprandial glucose control may specifically benefit patients who have difficulty in limiting postprandial glucose excursions.





## Jet injection for insulin administration may especially benefit subjects with higher BMI



In a euglycaemic glucose clamp study with healthy volunteers it was shown that using jet injectors, rather than conventional pens, significantly improved the time-action profiles of rapid-acting insulin analogs. Here, it was investigated whether such profiles were modified by body mass index (BMI) and related weight parameters by comparing insulin administration by jet injection to that by conventional pen in subgroups defined by BMI, waist-to-hip ratio, waist circumference and insulin dose.

After conventional administration, times to peak insulin levels (T-INSmax) occurred 31.1 [95% confidence interval (CI) 13.7–48.5] minutes later and time to maximum glucose requirement (T-GIRmax) 56.9 (95%CI 26.6–87.3) minutes later in more obese (BMI > 23.6 kg/m<sup>2</sup>) than in lean subjects (BMI < 23.6 kg/m<sup>2</sup>). In contrast, T-INSmax and T-GIRmax were similar in subjects with high and low BMI, when insulin was administered by jet injection.

It was concluded that using jet injection for insulin administration may especially benefit subjects with higher body weight.



## Jet injection advances the pharmacodynamics of regular insulin to that of an analogue

Rapid-acting insulin analogues are generally preferred over regular human insulin, because of their more immediate onset of action and shorter timeaction profile. However, these analogues may not always be tolerated by or universally available for people with insulin requiring diabetes.

Jet injection has been demonstrated to facilitate faster insulin absorption. We determined whether administration of regular human insulin by jet injection achieves the same pharmacological properties as that of a rapid-acting insulin analogue in 20 healthy volunteers.

Regular human insulin by jet injection had a faster onset of glucose-lowering effect compared to aspart by conventional pen (T-GIR50%,  $30.8 \pm 2.9$  versus  $43.1 \pm 3.2$  min,  $P < 0.01$ ). There were no differences in time to maximal GIR ( $106.1 \pm 11.9$  versus  $95.8 \pm 9.2$  min,  $P = 0.50$ ), maximal GIR ( $8.6 \pm 0.7$  versus  $7.7 \pm 0.7$  mg/kg/min,  $P = 0.0.33$ ), total glucose-lowering effect ( $101.0 \pm 9.8$  versus  $87.6 \pm 7.0$  g,  $P = 0.28$ ), and time until 50% of glucose disposal ( $144.8 \pm 5.6$  versus  $151.3 \pm 5.1$  min,  $P = 0.39$ ).

Jet-injected regular human insulin had a pharmacological profile that was essentially not dissimilar from that of aspart insulin administered by conventional pen, and can therefore be used as an alternative for conventionally administered rapid-acting insulin analogues and may help to achieve better meal insulin coverage and correction of postprandial glucose excursions.



## Technology improves Pharmacokinetic and Pharmacodynamic Profile of Rapid-Acting Insulin

Results showed that the time to maximal GIR was significantly shorter when insulin was injected with the jet injector, compared with conventional pen administration. The time to peak insulin concentration was similarly reduced and peak insulin concentrations were increased. Jet injector insulin administration reduced the time to 50% glucose disposal.

No differences were measured in maximal GIR, total insulin absorption, or total insulin action between the two devices.

Conclusions were drawn that administration of insulin aspart by jet injection enhances insulin absorption and reduces the duration of glucose-lowering action.

This profile resembles more closely the pattern of endogenous insulin secretion and may help to achieve better meal insulin coverage and correction of postprandial glucose excursions.



## References:

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4. Factors Affecting the Absorption of Subcutaneously Administered Insulin: Effect on Variability”, *Journal of Diabetes Research*, vol. 2018, Article ID 1205121
5. Insulin administered by needle-free jet injection corrects marked hyperglycaemia faster in overweight or obese patients with diabetes.  
Helana M. de Wit, Elsemiek E.C. Engwerda, Cees J. Tack, B.E.de Galan, *Diabetes, Obesity and Metabolism* 2015
6. *Diabetes Care* 1988 Jan; 11(1): 41-45

### Intended use:

The InsuJet™ insulin-jet administration system is intended for the subcutaneous jet injection of insulin in adults and children with Diabetes Mellitus who require insulin therapy.

### Intended user:

Licensed health care professional (HCP) or self-injecting patients or caregivers after proper training obtained from HCP.

### Cautions:

- Consult instructions for use before using this device.
- Consult a healthcare provider about your medical condition and appropriate treatment. Always follow the medication manufacturer’s instructions for use, contraindications, warnings, and precautions.

### For more information, please contact:



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