

Insujet^m Inject Needle-Free

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 needlephobia. 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.

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 varies clinical investigations of the InsuJet^(2,3).

This is mainly due to slower onset and offset of action of

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

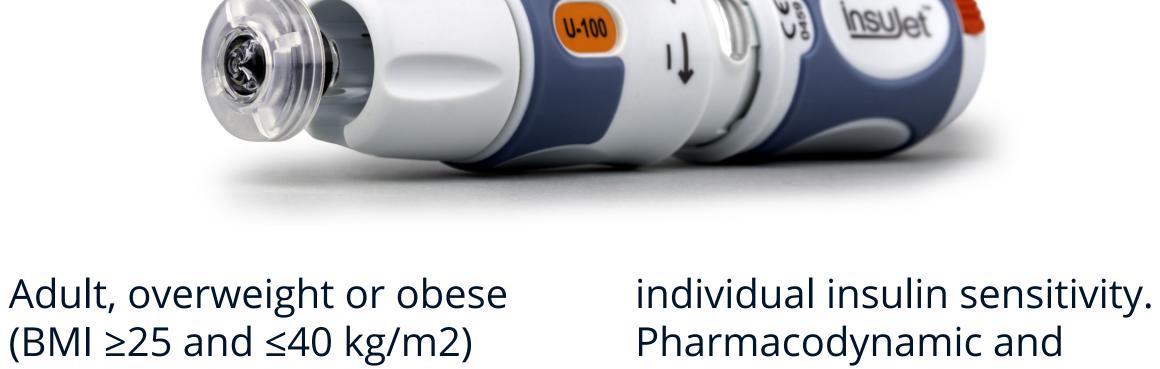
injection technique, low fat percentage and incorrect needle length.

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.

free jet injection corrects marked hyperglycaemia faster in overweight or obese patients with diabetes

Insulin administered by needle-



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

pharmacokinetic profiles were derived from plasma glucose and insulin levels, measured for 6 h 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.

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. Improved Early Postprandial Glucose

The studies show that the application of insulin by the InsuJet

Control compared with conventional Clamp studies have shown that the absorption and action of administration. Jet injection 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

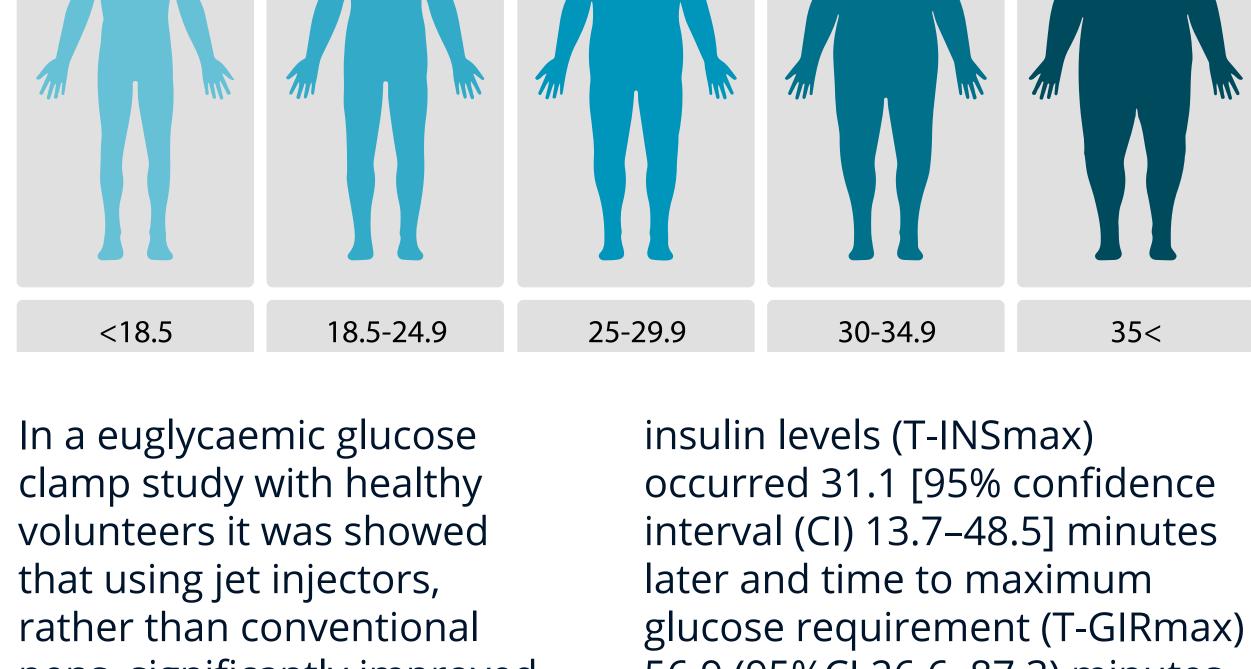
did not, however, significantly reduce the hyperglycemic burden during the 5-h period thereafter. There was no indication that the jet injector performed differently in patients with type 1 and type 2 diabetes. It was concluded that the considerably more rapid insulin

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.



administration may especially benefit subjects with higher BMI

Jet injection for insulin



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

56.9 (95%CI 26.6–87.3) minutes later in more obese (BMI > 23.6 kg/m2) than in lean subjects (BMI $< 23.6 \text{ kg/m}^2$). 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

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 insulinrequiring 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

Rapid-acting insulin analogues

regular human insulin because

are generally preferred over

conventional pen (T-GIR50%, 30.8 ± 2.9 versus 43.1 ± 3.2 min, P < 0.01). There were no differences in time to maximal GIR (106.1 ± 11.9 versus $95.8 \pm 9.2 \text{ min, P} = 0.50),$ maximal GIR (8.6 ± 0.7 versus $7.7 \pm 0.7 \, \text{mg/kg/min}, P = 0.0.33),$

glucose disposal (144.8 \pm 5.6 versus $151.3 \pm 5.1 \text{ min}$, P = 0.39). Jet-injected regular human insulin had a pharmacological profile that was essentially not dissimilar from that of

total glucose-lowering effect

aspart insulin administered

by conventional pen, and

 $(101.0 \pm 9.8 \text{ versus } 87.6 \pm 7.0 \text{ g},$

P = 0.28), and time until 50% of

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.





improves Pharmacokinetic and Pharmacodynamic Profile of Rapid-**Acting Insulin** InsuJet™ 's clinical trials, administration reduced the performed by a renowned time to 50% glucose disposal. Dutch academic hospital, No differences were measured

of administration of insulin aspart by jet injection to that by conventional insulin pen. 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

were performed to compare

the pharmacologic profile

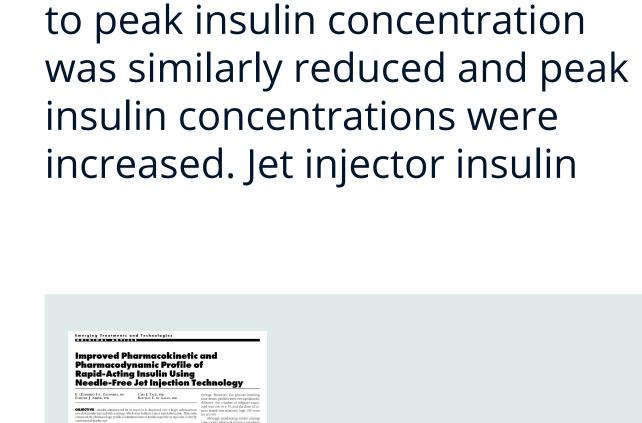
absorption, or total insulin action between the two devices. Conclusions were drawn that administration of insulin aspart by jet injection enhances insulin absorption and reduces the duration of glucose-lowering

in maximal GIR, total insulin

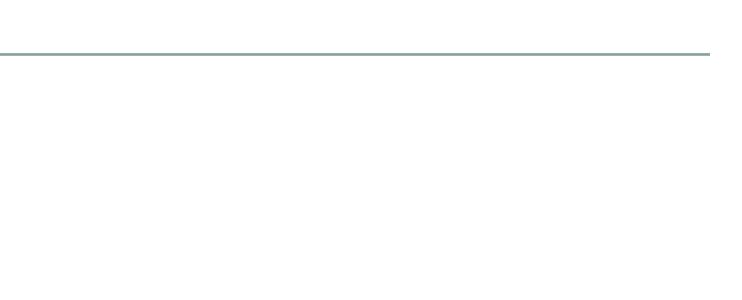
action. This profile resembles more closely the pattern of endogenous insulin secretion and may help to achieve better meal insulin coverage and correction of postprandial glucose excursions.











MEDICAL DEVICES

References: 1. Peyrot M, Rubin RR. Levels and risks of depression and anxiety

590

2. Improved pharmacokinetic and Pharmacodynamic profile of rapidacting insulin using needle-free injection technology. E.E.C Engwerda, E.J. Abbink, C.J. Tack, B.E. de Galan. Diabetes Care

Publish Ahead of Print, published online June 29, 2011

symptomatology among diabetic adults. Diabetes Care 1997; 20:585–

3. Needle-Free Jet Injection of Rapid-Acting Insulin Improves Early Postprandial Glucose Control in Patients With Diabetes technology. E.E.C Engwerda, E.J. Abbink, C.J. Tack, B.E. de Galan. Diabetes Care Publish Ahead of Print, published online October 2, 2013 4. Factors Affecting the Absorption of Subcutaneously Administered

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

Insulin: Effect on Variability", Journal of Diabetes Research, vol. 2018,