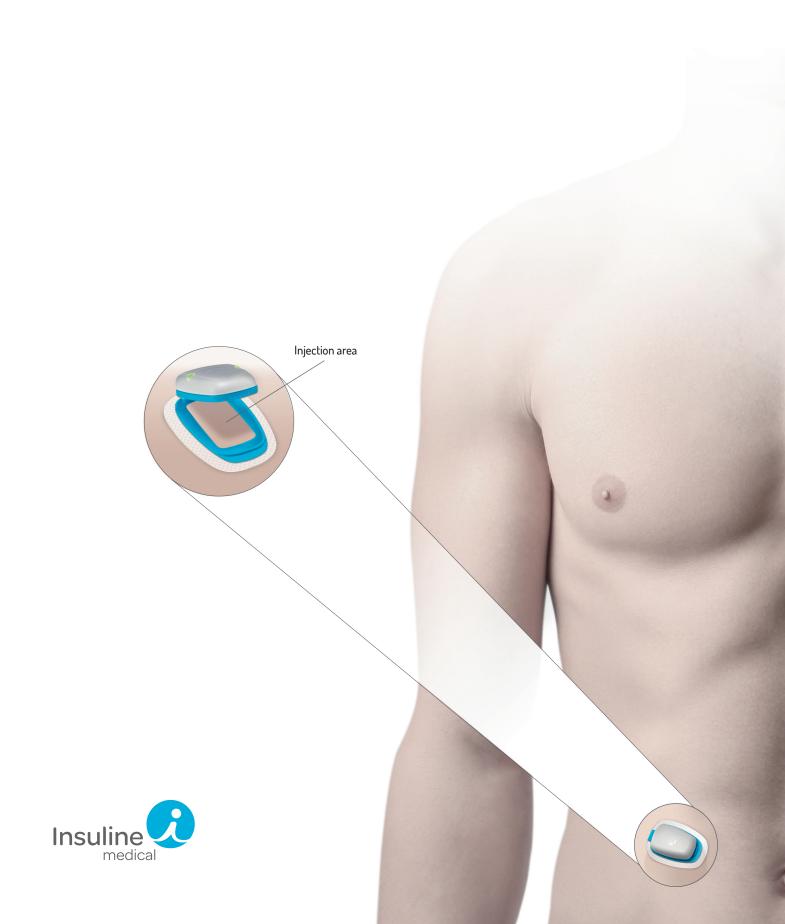
Take Control with InsuPad®

Achieve therapeutic target with less hypoglycemia and less insulin



THE CHALLENGE

- Worldwide, there are millions of diabetes patients treated with multiple daily injections therapy
- Insulin-dependent diabetes patients must constantly monitor their glucose levels and must adjust their insulin dose according to their food intake
- · Subcutaneous insulin delivery is:
 - Slow compared to normal physiology, resulting in high postprandial glucose levels
 - Associated with a high level of variability, depending on site of injection,
 local blood flow, local temperature and level of physical activity



Increased blood glucose variability



Increased rate of hyper- and hypoglycemic events

THE SOLUTION-InsuPad®*

- ✓ Achieves HbA1c goal similar to Standard of Care**
- ✓ Reduces the hypoglycemia event rate by 46%
- ✓ Reduces the required prandial insulin dose by 28%
- ✓ Reduces postprandial blood glucose excursions
- ✓ Innovative Skin Temperature Stabilization (STS) technology
- ✓ Non-invasive, safe, simple and easy to use



^{*}The claims are based on the BARMER [1] and MTT [2] studies which are further detailed in this document

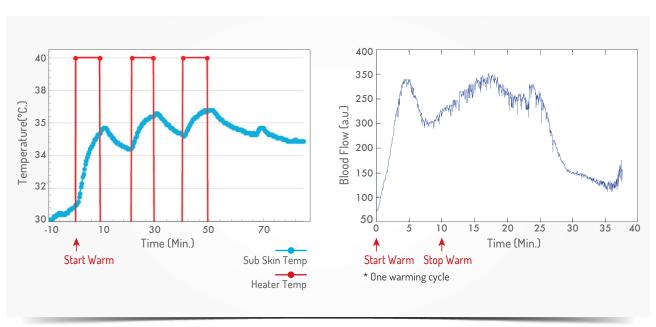
^{**}Standard of Care as used in the BARMER Study

STS innovation enables controlled and consistent insulin injection site conditions.

- Warms the skin surface of the insulin injection site to 40°C, after the injection
- There are three warming cycles of ten minutes each, followed by a ten minutes break in warming
- This leads to a local increase of cutaneous blood flow caused by the skin temperature regulation mechanism
- · Cycles cause consistent, stronger and longer-lasting increase of blood flow
- Increased local blood flow enables consistent and efficient insulin delivery from the subcutaneous site

InsuPad® heating profile

InsuPad® rapidly increases local blood circulation*



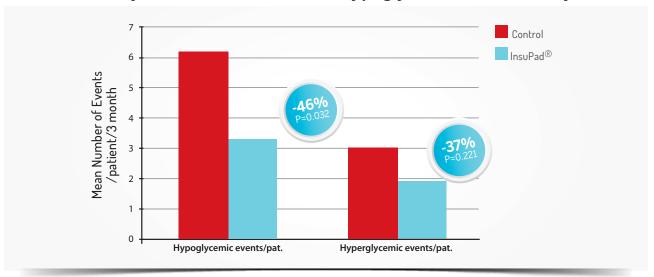
Measured sub-skin temperature in response to InsuPad $^{\circledR}$ warming

Measured local blood flow in response to 10 minutes of InsuPad®



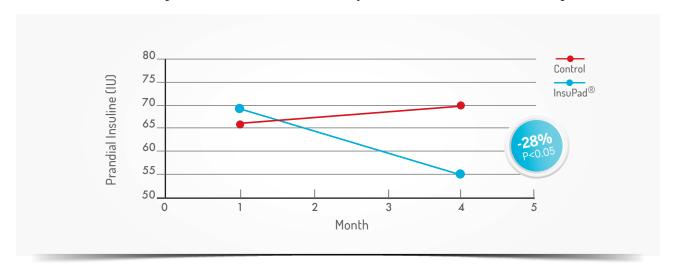
InsuPad®'s clinical efficacy and safety has been evaluated in multiple clinical studies with over 200 Type I & Type II diabetes patients.

BARMER Study: InsuPad® Reduces the hypoglycemia event rate by 46% [1]



Study Design (BARMER Study): Open-label, randomized, parallel, comparative study to assess efficacy and safety of InsuPad[®]. 145 diabetic patients on intensified insulin therapy and high total daily insulin dose (> 0.6 IU/Kg) were enrolled to the study. After 4 weeks of the treatment optimization period, patients were randomized to continue therapy for 3 months without (Control group, 66 patients) or with the InsuPad[®] device (InsuPad[®]-group, 69 patients, data presented here from 135 patients who completed the study). Observation parameters included HbA1c, insulin dose, and frequency of hypoglycemia, body weight and adverse events.

BARMER Study: InsuPad® Reduces prandial insulin dose by 28% [1]

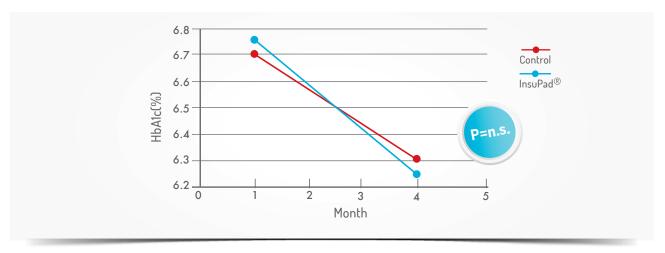


• In the **BARMER daily-life experience long term follow-up***, InsuPad® users reduced their prandial insulin dose by 32% over 18 months of use^[3].



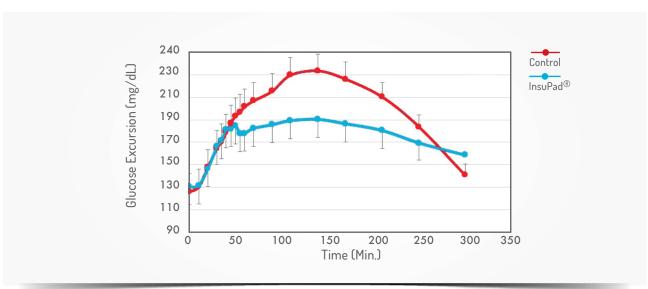
^{*}BARMER long term follow-up: 52 patients from one study site of the BARMER Study, irrespective of their prior randomization to InsuPad[®] or Control groups, chose to use the InsuPad[®] device daily for up to 18 months of follow-up (including the 3 months of the BARMER study).

BARMER Study: InsuPad® achieves HbA1c goal similar to Standard of Care [1]



• In the BARMER long term follow-up, InsuPad® maintained or further reduced HbA1c levels over 15 additional months of use

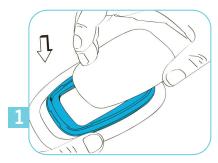
MTT Study: InsuPad® reduces post-prandial blood glucose excursions^[2]



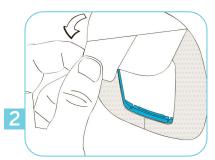
Study Design (MTT Study): Open-label, randomized, two-period, one-way crossover study to assess the effect of InsuPad® device on post meal glucose excursions during meal tolerance tests. 17 diabetes Type II patients underwent meal tolerance tests with a standardized liquid meal after an overnight fast on two study days. Subjects injected 0.2 U/kg of insulin Aspart or Lispro s.c. into the abdominal skin on both days, on one day followed by the use of InsuPad® and on the other day without. Blood samples for glucose measurements were taken from a venous line.

InsuPad is Non-invasive, safe, simple and easy to use

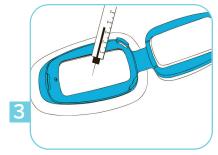
- Well tolerated. No serious adverse events (SAEs) were observed [1]
- Discreet and allows patients to continue with their daily activities
- Composed of a disposable injection window part (Fenster) and a reusable control unit. Both very easy to assemble



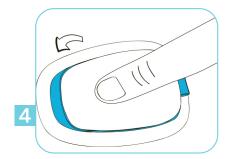
Simply assemble together a fully charged control unit and a new Fenster.



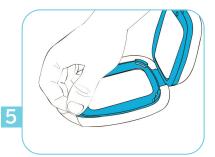
Attach the InsuPad® to the skin using the Fenster's adhesive tape.



To inject, open the disposable Fenster to reveal the skin injection area and inject within the Fenster's window.



Once the InsuPad® is closed (green indicator light), the warming cycle starts automatically. It then switches off automatically after 50 minutes.



At the end of the day or when the control unit's red indicator blinks and turn off, remove the InsuPad® from the skin and separate the Fenster from the control unit.



Charge the control unit and dispose of the used Fenster.

InsuPad® has won two prestigious international awards for its design





InsuPad® enables patients on intensive insulin therapy to take control of their disease and reach treatment targets in a more efficient and safer way.

InsuPad® is particularly recommended for use in diabetic patients with*[4]:

- · High prandial insulin requirements
- High prandial blood glucose excursions
- High blood glucose variability
- High risk of hypoglycemia

 BARMER Study: Patients were as satisfied with InsuPad® as with SoC, measured by the DTSQ* and PAID** scores^[4]

*Diabetes Treatment Satisfaction Questionnaire. **Problem Areas in Diabetes.

Use of the InsuPad®: Testimonials

P., P. (*1939, type 2 diabetic, qualified economist)

Before using the InsuPad®, my blood glucose values ranged from 76 mg/dl (4.2 mmol/l) to 378 mg/dl (21 mmol/l). Now my values range from 74 to 121 mg/dl (4.1 to 6.7 mmol/l). My improved blood glucose values also significantly improved my quality of life.

P., W.G. (*1945, type 2 diabetic, engineer)

I noticed a change in my diabetes management. The Pad is neither a physical nor psychological stress to me. There are no limitations when taking a shower or a bath. It is a genuine improvement for patients with diabetes!

0., M. (*1944, type 2 diabetic, qualified engineer)

First of all, I would like to mention my motivation, as I markedly lost weight within the first weeks. Furthermore, I had less appetite due to the smaller amount of insulin I had to inject. At the end of the study, I had lost 8 kg. My HbA1c ranged from 5.7% to 6.4% during the last nine months. Before the start of the study, I could only dream of these values.

Klaus Funke (MD)

Being a diabetologist, I was initially skeptical if a reduction of prandial insulin by 30 % can result in stable and good blood glucose values. At the telephone visit after 7 days, many patients reported that their blood glucose values were within the target range. Less hypoglycemic events occurred. Training patients how to use the InsuPad® was easy. Using the InsuPad® was reported as being uncomplicated and easy. Some patients were initially concerned about skin reactions. However, these did not occur.

Insuline

 $[\]star$ InsuPad $^{\circledR}$ should not be used when initiating prandial insulin treatment for the first time or in patients with consistent allergy to the plaster



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References:

- 1. Pfützner A., Funke K., Hermanns N. et al., The BARMER Study: impact of standardized warming of the injection site to enhance insulin absorption and reduce prandial insulin requirements and hypoglycemia in obese patients with diabetes mellitus. Curr. Med. Res. Opin., 30 (2014) 753–760.
- 2. Bitton G, Raz I, Pfützner A, Feldmann D, Alon T, Liviatan L, Nagar R. Reduced postprandial glucose excursion in type 2 diabetic subjects using the InsuPad device. Diabetologia 2012; 55(Suppl.1):A98
- 3. The BARMER Study Long Term Follow-up. Data on File
- 4. Pfützner A., Raz I., Bitton G. et al. Improved Insulin Absorption by Means of Standardized Injection Site Modulation Results in a Safer and More Efficient Prandial Insulin Treatment A Review of the Existing Clinical Data. J. Diabetes Sci. Technol. 2014 (accepted, in press)

To learn more about or to order InsuPad® I www.insuline-medical.com

