Insuline medical

InsuPad®

Fast and safe to therapeutic target

InsuPad®-System: Starter Kit and Components

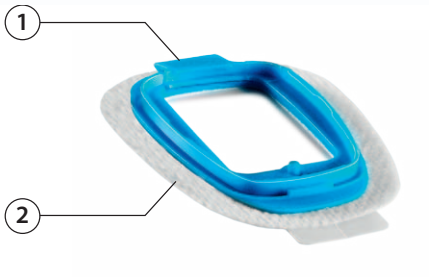
Starter Kit

The InsuPad® improves insulin absorption into the blood vessel system by selectively warming the injection site. The InsuPad® is suitable for patients with diabetes mellitus type 1 and 2 who inject rapid-acting insulins. The system consists of a set with InsuPad® "Fensters", a control unit, a charging base and a power adaptor.

Disposable "Fenster"

The disposable "Fenster" includes two parts:

1. A colored plastic cradle for connecting the control unit to the disposable "Fenster".
2. A biocompatible adhesive tape, intended for attaching the cradle and the control unit to the body. The unit is water-proof, and can be worn all day including e. g. under a shower.



Control Unit

The control unit is the core of the InsuPad® system. It controls and monitors all operational aspects of the system. The control unit includes a warming element, a thermistor for temperature monitoring and a rechargeable battery.

Charging Base and Power Adaptor

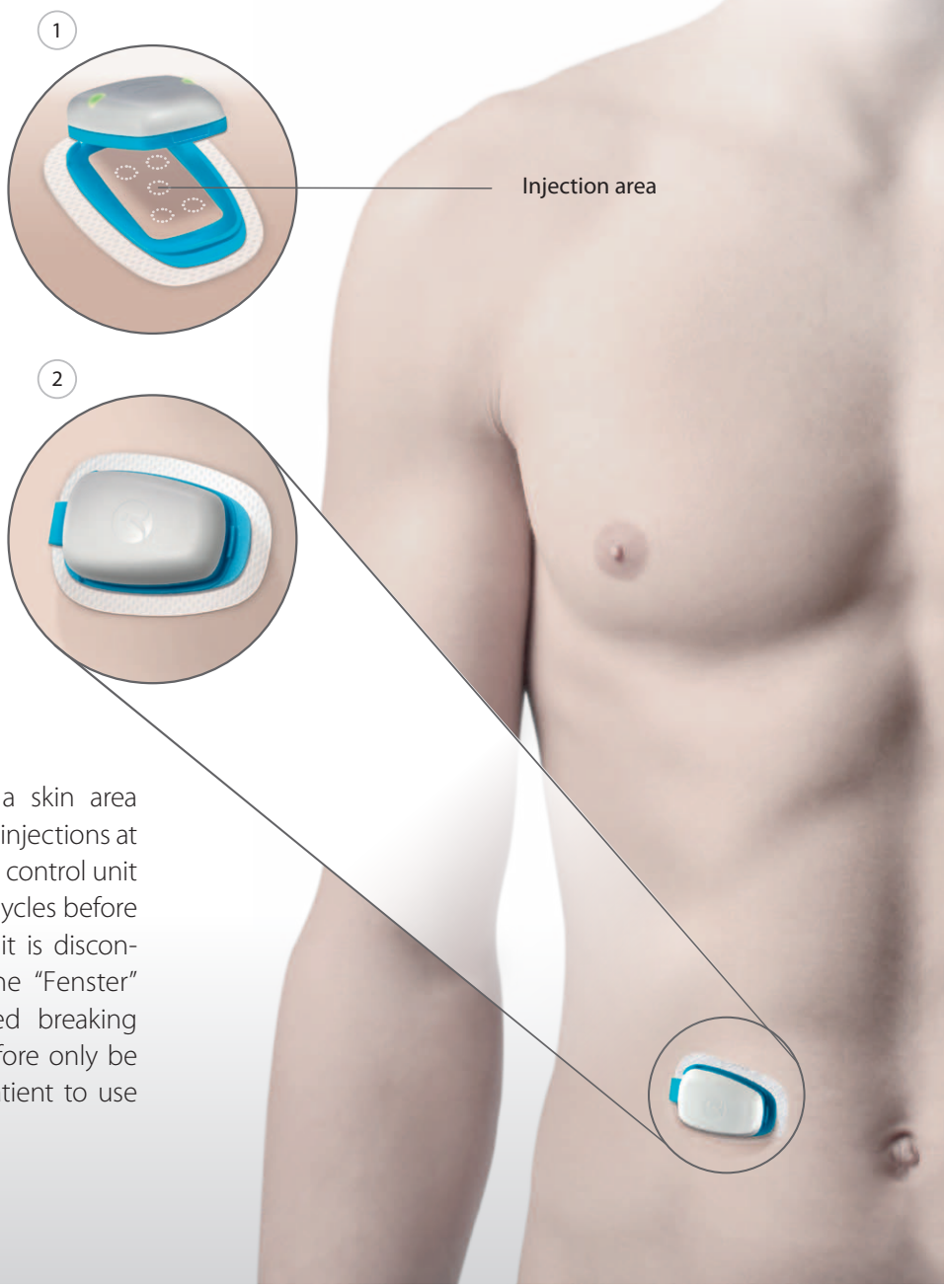
For charging, the control unit is attached to the charging base. By a USB cable, the charging base can be connected to all common power plugs and thus be used internationally.

Control Unit in Charging Base with Red Light Indicator

When the control unit is connected to the charging base, two red light indicators appear during charging phase. The charging takes approx. 90 minutes. When the unit is fully charged, the light indicators turn green. The charged control unit can then be connected to the disposable "Fenster".

Closed and Open Control Unit on a Disposable "Fenster"

The control unit which is connected to the disposable "Fenster" has a mechanism which controls the activation and de-activation of the warming cycle. If the InsuPad® system which is attached to the skin is opened (see picture 1), the green light indicators blink for some seconds. During this time, the system can be closed again without starting a warming cycle. If the system remains open, the indicators change to constant green light for approx. 60 seconds. Within this time, the insulin injection can be performed and the InsuPad® system has to be closed. After closing the system, the warming cycle is activated automatically and stops automatically after 50 minutes.



The opened InsuPad® system uncovers a skin area which is big enough to perform four to five injections at alternating injection sites. The fully charged control unit is capable to perform up to four warming cycles before having to be recharged. If the control unit is disconnected from the disposable "Fenster", the "Fenster" automatically torns at the predetermined breaking point. One disposable "Fenster" can therefore only be used for one day. This encourages the patient to use alternate injection sites.

BENEFITS AT A GLANCE

- **Improved diabetes control and simple application**

  Clinical studies with observational periods of 6 months have demonstrated that use of the InsuPad® markedly reduces postprandial blood glucose variability and thereby improves glycemic control of the patients in the long run [1].

- **Average reduction of hypoglycemic events by up to 45 %**

  Postprandial blood glucose variability is reduced.

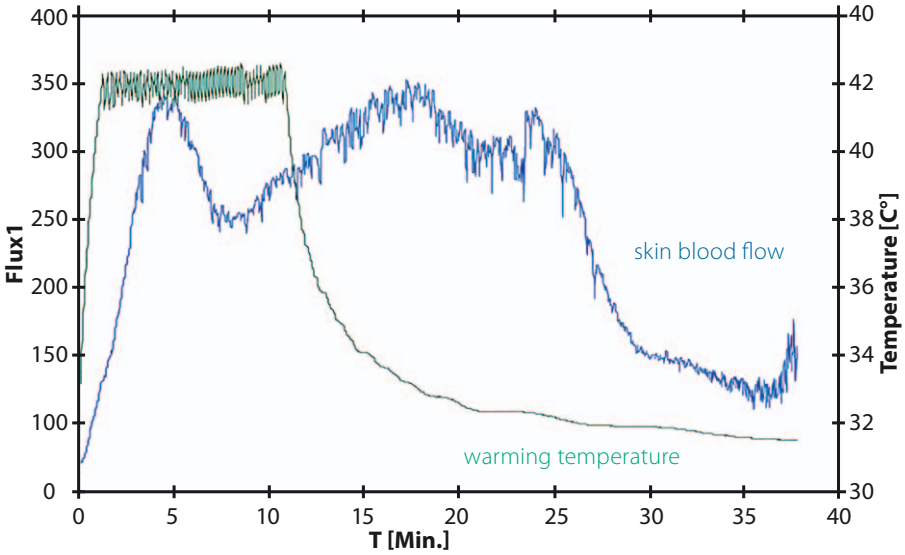
- **Average reduction of insulin consumption by up to 28 %**

  Normoglycemia at lower risk.

InsuPad®: Mechanism of Action

Effect of ten minutes of skin warming on local blood circulation of the skin

Increase of the surface temperature of the skin leads to a local increase of the cutaneous microcirculation caused by the skin temperature regulation. Using laserdoppler examinations, it was demonstrated that vasodilatation increases at 37 °C and reaches a plateau at 42 °C. If temperature increase is interrupted at this temperature, a rebound-effect takes place. The InsuPad® warms the injection site three times for ten minutes to 39.5 °C. Each warming is followed by a ten minute break. This cycle causes a stronger and longer-lasting increase of microcirculation than constant warming.



Study to Evaluate the Efficacy and Safety of the InsuPad® Device in Daily Life Conditions – the BARMER Study [1,2]

Primary Measure

The primary aim of the study was to demonstrate that patients who use the InsuPad® (test group) need less prandial insulin than patients who do not use the InsuPad® while having comparable HbA1c-levels (glycemic control).

- Open, randomized, parallel, comparative study
- 145 participants / 135 evaluable participants
- Patients with intensified insulin therapy with insulin analogues (Lantus® + rapid-acting analogues) and high total daily insulin dose (> 60 IU)
- Competitive patient recruitment (13 German study sites)

Background

The study design of the BARMER study was developed in close cooperation with the German statutory health insurance BARMER GEK in order to collect data on the medical and pharma-economical aspects of the use of the InsuPad®.

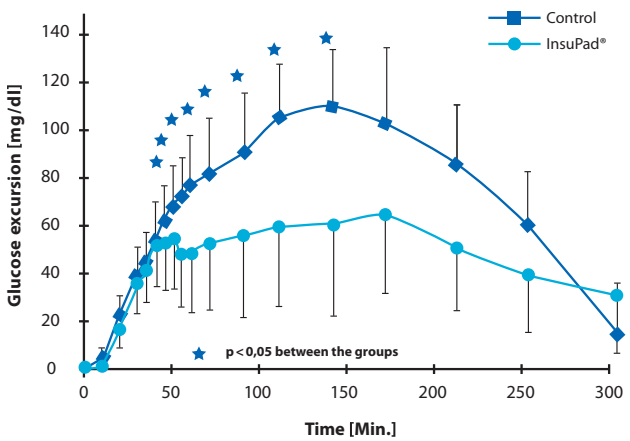
Results: Patient population at baseline (Full Analysis Set)

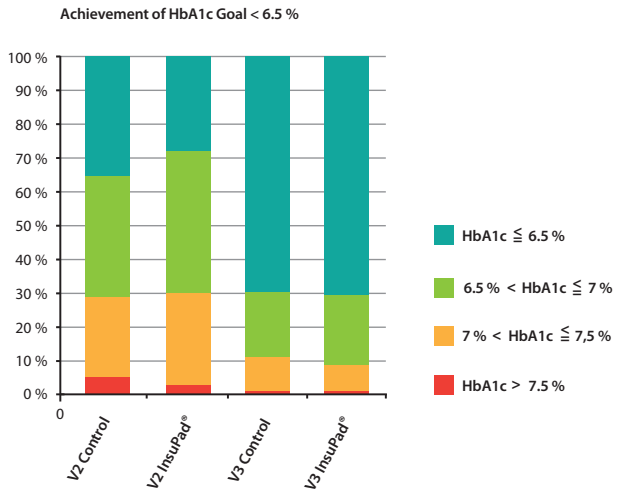
Parameter	All patients	Control Group	InsuPad®
N	135	66	69
Sex • male • female	 97 (64.4 %) 47 (35.6 %)	 41 (62.1 %) 25 (37.9 %)	 46 (66.7 %) 23 (33.3 %)
Ethnic Origin • Caucasian • Asian	 99.4 % 0.6 %	 100.0 % 0.0 %	 98.6 % 1.4 %
Diabetes type • Type 1 • Type 2	 13 (9.6 %) 122 (90.4 %)	 7 (10.6 %) 59 (89.4 %)	 6 (8.7 %) 63 (91.3 %)
Age (years)	61 ± 8	62 ± 8	61 ± 9
Diabetes duration (years)	17 ± 7	17 ± 7	16 ± 8
Weight (kg)	105.7 ± 18.5	103.8 ± 16.8	107.6 ± 20.1
BMI (kg/m^2)	35.5 ± 6.1	34.9 ± 4.9	36.2 ± 7.1
HbA1c (%)	7.2 ± 0.5	7.2 ± 0.5	7.2 ± 0.5
Prandial Insulin **Insulin Lispro** **Insulin Aspart** **Insulin Glulisin**	 56 (41.5 %) 54 (40.0 %) 25 (18.5 %)	 33 (50 %) 24 (36.4 %) 9 (13.6 %)	 23 (33.3 %) 30 (43.5 %) 16 (23.2 %)

Rapid availability

Clinical efficacy

In a randomized 2-day crossover study 16 patients with diabetes mellitus type 2 received a standardized meal and injected the same insulin dose, once while using the InsuPad® and once without the InsuPad® (control). When using the InsuPad® device and at similar initial blood glucose values (approx. 120 mg/dl; 6,7 mmol/l respectively), a more pronounced reduction of postprandial blood glucose excursions was shown (refer to Figure, [3]).





HbA1c goal (< 6,5 %)

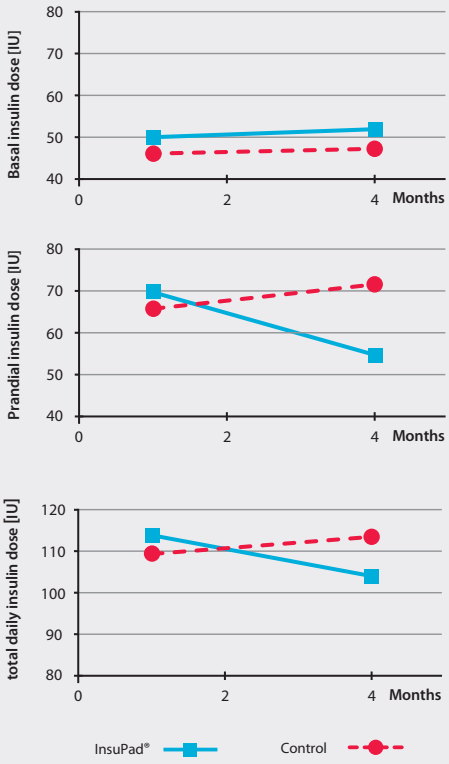
Distribution of patients in HbA1c categories at baseline and endpoint. Treatment to the target area < 7.0 % was achieved in approx. 90 % of the participants in both groups [1].

Insulin dose

In order to achieve such an excellent level of glycemic control, patients of the control group had to increase their prandial insulin dose by **8.1 %** (66 ± 32 IU to 71 ± 38 IU, $p < 0.05$), while the basal insulin dose remained stable. In contrast, patients of the InsuPad® group needed markedly less prandial insulin than before (70 ± 43 IU to 55 ± 34 IU, **-19.4 %,** $p < 0.001$), but had a slight increase in basal insulin.

The required economic benefit by saving at least 10 % of the prandial insulin dose at comparable glycemic control by using the InsuPad® was exceeded: the final value of the saving was 27.5 %.

As a result, the total daily insulin dose increased by 3.7 % in the control group and decreased by 8.6 % in the InsuPad® group ($p < 0.001$, see Figure on the right). **It is recommended to reduce the prandial insulin dose by 30 % when starting a therapy with the InsuPad®.**



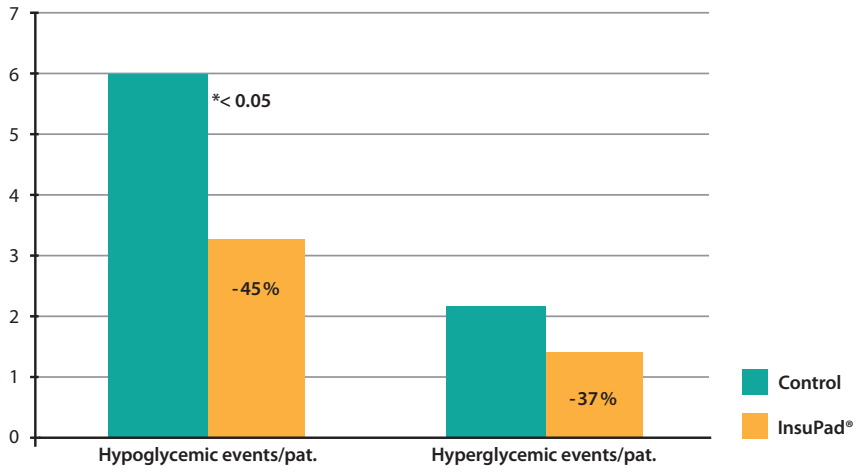
Treatment satisfaction

In general, using the InsuPad® led to higher treatment satisfaction. Increased diabetes-associated distress was not reported. The patients noticed a better blood glucose control. The frequency of extreme blood glucose values was significantly reduced. Subjectively reported pain decreased in the InsuPad® group [2].

Safety

During the observational period 15 serious adverse events were reported (control group: eight events, test group: seven events). In most cases these were hospitalizations due to known concomitant diseases. In both groups, moderate hypoglycemic events were reported. **No serious adverse event reported in this study was associated with the use of the InsuPad®.**

Frequency of hypoglycemic (< 63 mg/dl; < 3,5 mmol/l) and hyperglycemic (>250 mg/dl; >13,9 mmol/l) event



Conclusion

The InsuPad® is a new option to improve the efficacy and safety of insulin therapy in patients with diabetes mellitus type 1 or 2. Patients of the InsuPad® group had a similar glycemic control with lower prandial insulin demand and showed a significant reduction of hypoglycemic events.

References

1. BARMER Study: Pfützner A., Funke K., Hermanns N. et al., Diabetologia, 56 (Suppl.1): A437, 2013
2. Treatment Satisfaction Assessment: Pfützner A., Hermanns N., Kulzer B. et al., IDF Conference, Melbourne 2013
3. Study performed by Prof. Itamar Raz, Hadassah School of Medicine, Jerusalem, Israel: Pfützner A., Feldmann D., Bitton G. et al., Diabetes Technol. Ther., 15 (Suppl.1): A86, 2013

Experience with the InsuPad®

Klaus Funke, MD, investigator

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 seven 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® did not result in problems. Using the InsuPad® was assessed as being uncomplicated and easy.

Some patients were initially concerned about skin reactions. However, these did not occur. Especially female InsuPad® users reported that the adhesive tape even stuck to the skin while going to the sauna. The study team and the InsuPad® users were enthusiastic about the possibility to reduce the insulin demand, consecutively reducing the number of hypoglycemic events and a moderate, in single cases even considerable weight loss.

Conclusion:

The InsuPad® should be implemented into daily practice as soon as possible.

Use of the InsuPad®: Testimonies of Patients with Diabetes

*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 physical nor psychical stress to me. There are no limitations when taking a shower or a bath. It is a genuine improvement for patients with diabetes!

*O., 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 study start, I could only dream of these values.

The following table summarizes my most important values:

Study	Humalog	Lantus	Total dose	Oral anti-diabetic	Weight
Start: June 01, 2012	130 IU	110 IU	240 IU	2 tablets	138 kg
End: September 30, 2012	45 IU	100 IU	145 IU	2 tablets	130 kg
8 months later	75 IU	80 IU	155 IU	2 tablets	126 kg

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