



# Insulin Dependent Diabetes Trust

Looking After Your Insulin



It is over 75 years since the discovery of insulin and there is now a variety of insulins available, all of which are highly purified. It is important that the insulin we use is safe and effective so that the insulin itself is not responsible for varying blood glucose levels.

- Fact - Insulin is a powder that is mixed in solution and once in solution it breaks down slowly into insulin transformation products [ITPs].
- Fact - There is a slow rate of breakdown or transformation when insulin is stored in the refrigerator at 4°C
- Fact - This breakdown is accelerated by exposure to light, heat and agitation or regular shaking.
- Fact - Increasing the purity of insulin reduces its stability.

## **Warning!**

To ensure that your insulin remains effective, stable and undamaged

you should discard your 'in use' insulin after 28 days as a necessary precaution.

Insulin has a 'use by' date as well as an expiry date. This is general advice and specific insulins may have different times so you should always check the Patient Information Leaflet inside your insulin pack.

Diabetes is not an easy condition to live with and control of blood glucose levels can be difficult. The reasons for this are:

1. There are no insulins available that mimic the body's insulin production in response to food intake.
2. People with diabetes are all individuals with different hormonal and metabolic rates so each person responds to insulin in a different way.
3. There are many variables that affect diabetic control such as: diet,

exercise, lifestyle, fears of low blood sugars [hypos], emotions and stress.

Diabetes will remain a difficult and complex condition until we are provided with better 'tools' to control it. Therefore, it is important that we rule out factors that may result in more erratic blood glucose levels. This must include the possibility that our insulin has broken down making it less potent and therefore affecting blood glucose levels differently. Remember, if using 'old' insulin it may have lost some of its potency and a change to a new fully effective vial or cartridge could result in hypoglycaemia at the changeover time.

### **How long do people use their insulin?**

A study carried out in 1991 showed that people used a vial of insulin for about 4 to 13 weeks. IDDT asked 40 people how they stored their insulins.

- The vast majority of them stored their unopened insulin in the fridge and 75% of them kept their opened insulin out of the fridge.
- The majority used their short acting insulin in less than 4 weeks but they used their longer acting insulin for 6 to 12 weeks and most of them kept it out of the fridge.
- Almost everyone used their insulin down to the very last drop and only one person had been told by their doctor/nurse to discard their insulin after 28 days.

**Remember before using cloudy long-acting insulin, it should be gently rolled to ensure that the insulin mix is even.**

### **Confusion over in- use dates of insulins!**

#### **When should you discard your in-use insulin?**

A joint letter from physicians in Diabetes Care [Vol 26;9:2665-2669 Sept 03] expressed concern about conflicting information on insulin in-use dates and that the information from different sources is contradictory. Diabetes Care considered this issue to be of such clinical relevance that the insulin manufacturers were asked to make

statements for publication. IDDT then found that this information varied considerably with information for the same products in the US and the UK! Therefore we are also including on our charts the in-use times for insulin products in the US, where known. We hope that this provides a more informed choice for people using insulin.

### **Information from the insulin manufacturers**

#### **Novo Nordisk Pharmaceuticals Ltd**

In 2001 Novo Nordisk UK provided the following information to IDDT: *"Our unopened insulins are stable until the expiry date if stored in a refrigerator. Once open vialled insulin is stable for up to 3 months in the refrigerator and 6 weeks at 25°C. Insulin in cartridges is stable for up to 4 weeks once opened if stored at 25°C; we do not recommend that in use cartridges are stored in the refrigerator."*

However, this information differs from that provided to IDDT in 2003 by the company for the times and temperatures. It also differs from the Summary of Product Characteristics and with that provided to Diabetes Care! So we can only suggest that ***you*** decide which recommendations to follow!

**In-use storage of Novo Nordisk insulin preparations taken from the current UK Summary of Product Characteristics (SPC) for each product**

<b>Insulin</b>	<b>Vial</b>	<b>Penfill®</b>	<b>FlexPen®</b>	<b>NovoLet®</b>	<b>InnoLet®</b>
Synthetic GM					
NovoRapid® [Analogue]	4 weeks up to 30°C <i>[US, 28 days]</i>	4 weeks up to 30°C <i>[US, 28 days]</i>	4 weeks up to 30°C <i>[US, 28 days]</i>	Not available	Not available
NovoMix® 30 [Analogue]	Not available	4 weeks up to 30°C <i>[US, 14days]</i>	4 weeks up to 30°C <i>[US, 14days]</i>	Not available	Not available
Levemir®	Not available	6 weeks up to 30°C	6 weeks up to 30°C	Not available	Not available
Actrapid®	6 weeks up to 25°C	6 weeks up to 30°C <i>[US, 28days]</i>	Not available	6 weeks up to 30°C <i>[US, 28 days]</i>	Not available
Insulatard®	6 weeks up to 25°C	6 weeks up to 30°C <i>[US, 14 days]</i>	To be discontinued	To be discontinued <i>[US, 14 days]</i>	To be discontinued <i>[US, 14 days]</i>
Mixtard 30	6 weeks up to 25°C	6 weeks up to 30°C <i>[US, 10 days]</i>	Not available	6 weeks up to 30°C <i>[US, 10 days]</i>	6 weeks up to 30°C

**Note!**

- The information in italics applies to the US and was obtained from Diabetes Care. Please note that the in-use dates of the equivalent insulins in the US are shorter than advised in the UK. This appears to apply to analogues and to the longer-acting insulins
- In the US it is recommended that NovoLog [NovoRapid in the UK] in pump reservoirs is to be discarded after no more than 48 hours of use or after exposure to temperatures that exceed 37°C.

**Eli Lilly**

**Lilly's statement in Diabetes Care in the US is for synthetic human and analogue insulins.**

**Unopened:** Vials, cartridges and pre-filled pens may be used to the expiry date on the pack when stored in the refrigerator at 2-8°C.

**In-use:** the recommendations vary according to the insulin formulation,

its container [eg vial or cartridge], the temperature and the regulatory requirements. The Committee for Proprietary Medicinal Products state that insulin is like other sterile products and has a proposed maximum in-use period of 28 days and also that it must retain 95% of its labeled potency.

Humulin vials should be discarded after 28 days but the in-use dates for cartridges and pre-filled pens is shorter than for vials due to reduced volumes, increased agitation and potentially variable temperature exposure of a cartridge or pre-filled pen. In-use cartridges should be kept at room temperature and should NOT be kept in the refrigerator. In 2001 Diabetes Interview, a US publication, provided information from Lilly stating that pens kept at room temperature both opened and unopened should be discarded after the following number of days:

- Humulin 1 pen [isophane] - 14 days
- Humulin 30/70 pen - 10days
- Humalog 25/75 Mix - 10 days

**UK information is not the same!**

The Summary of Product Characteristics [SPCs] in the UK for ALL Lilly insulins gives the in-use date of 28 days regardless of insulin type or container ie vial, cartridge or pre-filled pen.

**Sanofi - Aventis**

**Lantus [insulin glargine]**

Unopened vials: should be stored in refrigeration at 2-8°C. If refrigeration is not available, then unopened insulin should be discarded after 28 days and both unopened and in-use vials and cartridges must be kept away from direct heat and light.

**Opened vials:** the Summary of Product Characteristics states that in-use Lantus in vials, cartridges and pre-filled pens MUST be discarded after 28 days whether refrigerated or not. It also says that it must not be stored above 25oC. [This could prove difficult in hot climates or even the UK summer.]

**Apidra [Short-acting Insulin analogue]**

**Unopened vials:** should be stored in refrigeration at 2-8°C. Keep the vial, cartridge and pre-filled pen in the outer carton in order to protect from light.

**Opened vials:** the Summary of Product Characteristics states that in-use Apidra in vials, cartridges and pre-filled pens have a shelf life of 28 days.

**In-use storage of Sanofi-Aventis insulin preparations taken from the current UK Summary of Product Characteristics (SPC) for each product**

Insulin	Vials	Cartridges	Optiset Pen
Lantus® [Analogue]	4 weeks - do not store above 25°C	4 weeks - do not store above 25o°C	4 weeks - do not store above 25°C
Apidra [Analogue]	4 weeks - do not store above 25°C	4 weeks - do not store above 25°C	4 weeks - do not store above 25°C

**Wockhardt UK [formerly CP Pharmaceuticals Ltd]**

“A single vial may be used repeatedly over a 3 month period, as long as the vial is maintained at the correct storage temperature of 2 to 8°C ie in the refrigerator. If the vial is stored outside the refrigerator [at room temperature] then this period of use should be reduced to 28 days. This also assumes that the vials are appropriately stored and are used under normal conditions ie that is to avoid microbial contamination. Insulin in cartridges is stable for up to 4 weeks once open, if stored at 25oC. We do not recommend that ‘in use’ cartridges are stored in the refrigerator.”

The Summary of Product Characteristics for ALL Wockhardt insulins says that following the first dose, it is recommended that the insulin is discarded after 28 days. Chemical and physical stability of in-use insulin has been demonstrated at 25°C for 28 days.

All the manufacturers of synthetic GM insulins recommend that stored insulin and in-use insulin vials are kept in their outer carton to protect the insulin from light and that caps are kept on pens when not in-use for the same reason.

### Long-term storage of insulin

IDDT collects unwanted in-date insulin to send to developing countries where insulin is unaffordable for many poor people, so it is important to know how long this donated insulin can be stored and still maintain its potency. However, this is no longer just an issue for developing countries as discontinuation of animal insulins in many countries has resulted in people who cannot tolerate synthetic GM insulins buying in large stocks of animal insulin. But what about the expiry date and how long will this stored insulin remain potent and effective at lowering blood glucose levels?

### Expiry dates

According to the International Diabetes Institute, which incorporates the World Health Organisation Centre for Diabetes and Health Promotion, insulin manufacturers are required to place an 'expiry date' on each container of insulin but this date appears to be a nominal one, not based on available scientific evidence. The expiry date is usually 2 years after manufacture but varies between manufacturers and between countries. [ref1] The date is determined partly by commercial considerations but it also allows for a margin of error when storage conditions by the dispenser and consumer are unknown.

**Note** - like food labeling, the expiry date does mean that you, the patient, would have no legal redress if you used 'out of date' insulin and anything went wrong. IDDT recommends that you follow the manufacturer's instructions.

### Insulin potency

Potency is the effectiveness of insulin to lower blood glucose. Potency decreases with exposure to light, temperature and vibration, so correct storage of your insulin is important. In-use insulin not stored in the fridge has been exposed to all these factors so its potency may be reduced and this is why it should be discarded after 28 days [less with certain insulins].

The following facts are known [ref1]

- The potency of insulin decreases very gradually over time and the degree of reduction depends on the storage conditions.
- Insulin should be stored in the dark as exposure to sunlight decreases its biological activity. The optimum storage is in the dark at temperatures between 2 and 8°C. Freezing must be avoided as it can destroy the insulin.
- If there is a loss of potency as a result of storage at high temperatures for long periods, then the breakdown products of insulin are not harmful in any way - unlike expired antibiotics, for example. So the insulin is safe to use but it may not be fully effective.

The table below shows the extremely long periods of time before the potency is reduced by even small amounts – no similar figures are available for analogue insulins.

### Time of storage of insulin preparations at various temperatures until biological potency is reduced by 2% and 5% respectively

Insulin preparation	4°C	15°C	25°C	40°C
Actrapid	36/92 years	5/13 years	12/31 months	5/14 weeks
Semilente	45/115 years	4/11 years	7/18 months	2/5 weeks
Lente	36/91 years	3/9 years	5/14 months	1/ 4 weeks
Rapitard	22/55 years	3/8 years	7/17 months	3/7 weeks
Ultralente	19/48 years	2/5 years	4/10 months	1/3 weeks

Information source: 'Galenics of Insulin' by J Brange M.Sc et al: [Novo Research Institute, Denmark] Springer-Verlag, 1987

### In emergency situations

Provided insulin is stored appropriately, it may be used for several

years and certainly for at least 12 months after the nominated expiry date. This is particularly important when insulin is provided in an emergency situation in developing countries, as it can be lifesaving. It is also important for people in developed countries who have to store large quantities of animal insulin because they cannot tolerate the only insulin available to them, synthetic GM insulin. So, in emergency or necessity, it is unimportant whether the potency is 95% or 99% and in the unlikely event of the potency dropping to 90%, adjustment of the insulin dose would overcome the problem.

*Ref 1 Information on storage of insulin. Dr M Cohen, July 1996*

### **Holiday tips**

Going on holiday if you have diabetes means that you have to take a few extra precautions, especially if you are travelling overseas. Here are some tips to help you – ones that we have learnt by experience.

### **Looking after your insulin**

- Travelling overseas probably means that your insulin will not be kept in a refrigerator for days or even weeks. Exposing insulin to high temperatures can make the insulin weaker and so it will not act as efficiently.
- If a refrigerator is not available try to store the insulin in a cool dark place.
- Carry your insulin in a polystyrene container or a small wide necked vacuum flask.

There are also containers available with a cooling system of plastic containers filled with liquid that can be pre-cooled in your refrigerator. Do not pre-cool to the low temperature of a deep freeze because freezing can destroy the insulin. FRIO Wallets can be obtained from FRIO UK, Freepost SWC 0667, Haverfordwest, SA62 5ZZ.

### **Travel insurance**

From 2005 travel insurance sold by insurers and brokers will be regulated by the Financial Services Authority [FSA] but insurance bought with a holiday package will not. This could lead to confusion

and lack of protection, often because travel agents do not know the right questions to ask! A survey by Which? in 2001 found that only three out of 20 agents questioned asked about pre-existing medical conditions.

Two thirds of people buy their holiday insurance from travel agents rather than shopping around, especially as many agents refuse to accept the booking unless the cover is purchased as well. The lack of regulation for travel insurance through travel agents could mean that people are not receiving the protection they require.

Pre-existing medical conditions such as diabetes, are already a grey area for travel insurance with many people finding that when they make a claim the insurer will not pay up saying that the pre-existing illness or condition excluded them from the scope of the policy. These problems usually occur when the insurance is sold as part of a holiday package.

Each insurance company has its own criteria for judging medical conditions and in many cases the more serious the illness, the higher will be the premium and diabetes attracts a higher premium.

### **Best advice!**

Always check the small print of a policy to make sure that you and your diabetes are adequately covered. If you are not asked very detailed questions about your health then you should ask whether any of the conditions you have will affect the cover that is offered.

**New European Health Insurance Card** - from September 1st 2005 new cards have been issued, EHIC, which replace the existing E111 form. The benefits are the same - entitlement to reduced or free essential medical care while in EU countries and Switzerland. The EHIC does cover chronic conditions such as diabetes but it is advisable to have additional travel insurance.

### **Precautions when travelling by air**

- Make sure that your insulin is in your hand luggage in the cabin with you. The luggage hold of the aircraft will go below freezing due to the high altitude and this will destroy or damage your insulin.
- Carry two lots of insulin, testing equipment and syringes/pens and distribute them between two different hand luggage bags - you could give one set to your travelling companion. Luggage does get lost and it could prove difficult to replace your insulin or syringes/pens.
- Always carry a card to say that you have diabetes.
- As a result of increased security controls, you require a letter from your doctor to state that you have diabetes and need to carry syringes/pens and lancets with you on the flight.
- Remember to always take sufficient insulin with you because you may not be able to obtain your type of insulin in the country you are visiting. This is particularly important for people using animal insulins that are now unavailable in most countries.
- When you come home it is sensible to throw away any unused insulin that has travelled with you as it has been exposed to heat, bright light and to vibrations, all of which can damage insulin and make it less effective.
- If you are overseas for long periods and cannot obtain your usual insulin in that country John Bell and Croyden, Pharmacists, Wigmore Street, London will correctly pack and courier insulin [and other drugs] to you. They require a doctor's prescription, either NHS or private and payment by credit card. Alternatively, if you use Hypurin beef or pork insulins these can be obtained with a doctor's prescription directly from the manufacturers, Wockhardt UK [contact details are on your insulin pack].

Further information and advice about travelling and holidays can be obtained in IDDT's Leaflet, Holiday Tips and Travel Information.

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