

# A Guide to Successful Management of Diabetes Mellitus in Dogs and Cats



## Introduction

Diabetes mellitus is a common endocrine disorder of dogs and cats that results from an absolute or relative insulin deficiency. In general, the prognosis is good, provided that the diagnosis is made at an early stage and treatment is adequate.

Insulin treatment is the cornerstone of successful management, but appropriate diet and a regular lifestyle are also important. First-rate communication between you, the veterinarian and the pet owner is of major importance. Your attitude to diabetes mellitus will largely determine the owner's motivation and compliance with treatment.

## Incidence

Estimates of the incidence of diabetes mellitus in dogs is 1 in 300 and cats is 1 in 200 range.<sup>1,2</sup> Diabetes occurs most commonly in middle aged and older dogs and older cats. In dogs, there is a genetic factors lead to a higher incidence in breeds such as Keeshond, Beagle, Australian terrier, and Samoyed.<sup>3</sup> A higher incidence is seen in Burmese cats and in neutered male cats.<sup>3</sup>

## Etiology

Diabetes mellitus can originate from either pancreatic or non-pancreatic disease.

### ENDOCRINE

Destruction of endocrine pancreatic tissue can lead to diabetes mellitus. In dogs, there is some evidence that autoimmune destruction of the islets of Langerhans plays a role in the pathogenesis of diabetes. In cats, amyloid deposition may contribute to the destruction of the islets of Langerhans.

### EXOCRINE

Severe inflammation or neoplasia of the exocrine pancreas can also lead to loss of islet function. In these cases, diabetes is complicated by exocrine pancreatic insufficiency.



# Diabetes mellitus due to disease not primarily of pancreatic origin

## OVERPRODUCTION OF COUNTERACTING HORMONES AND INSULIN RESISTANCE - GROWTH HORMONE EXCESS

**Metestrus / pregnancy** - Progesterone produced during the luteal phase induces the production of growth hormone by the mammary gland. This counteracts the action of insulin and is seen in intact female dogs as well as following progestin administration to dogs or cats.

**Acromegaly** - Acromegaly (hypersomatotropism) is caused by growth hormone excess. This is not uncommon in cats where it is due to a growth hormone-secreting pituitary tumor.

## HYPERADRENOCORTICISM

Hyperadrenocorticism is a relatively common endocrine disorder in dogs. Corticosteroids stimulate gluconeogenesis, leading to an increase in the blood glucose concentration. This stimulates insulin synthesis.

## Glucose toxicity

Glucose toxicity occurs when insulin secretion is reduced by prolonged hyperglycemia. Prolonged hyperglycemia can be due to a number of causes including the ones listed below.



## IATROGENIC

**Corticosteroids** - The therapeutic use of corticosteroids can induce diabetes mellitus.

**Progestins** - The use of exogenous progestins can lead to growth hormone excess. Progestins also have an affinity for glucocorticoid receptors.

## OBESITY

In obesity, tissue receptors have decreased insulin sensitivity. This leads to a greater demand for insulin, which can result in exhaustion of the islets of Langerhans. In cats (but not in dogs), obesity has been shown to be a risk factor for the development of diabetes.

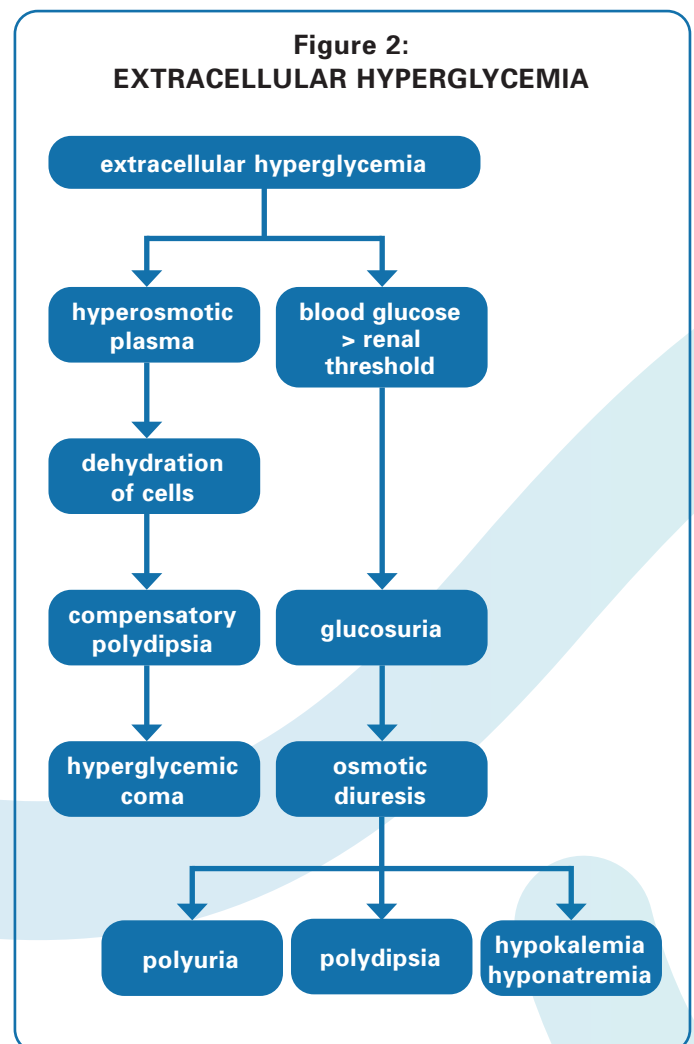
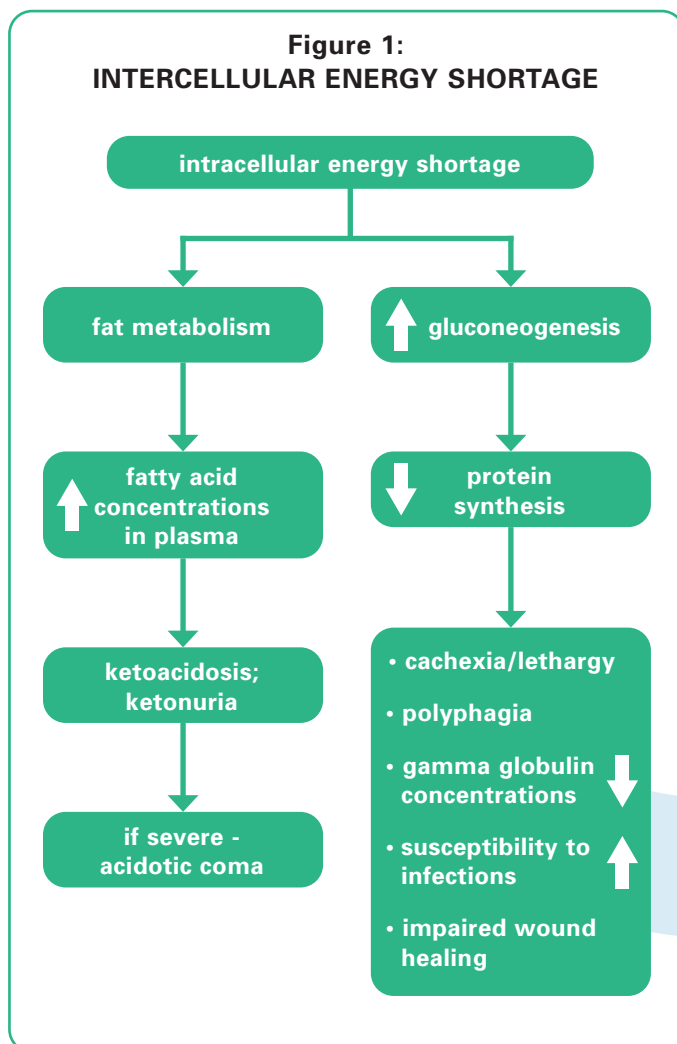
## Potential diabetes mellitus

Potential diabetes mellitus, defined as impaired insulin synthesis and/or decreased sensitivity of tissue receptors to the effects of insulin, results in an increased blood glucose concentration that does not yet exceed the renal threshold. This is seen in intact female dogs during metestrus. At this stage, the problem may still be reversible by spaying (elimination of the progesterone source).

Mild hyperglycemia may also be encountered in hyperadrenocorticism and reversal of the cortisol excess may prevent the development of diabetes mellitus.

## Pathogenesis

Diabetes mellitus is a paradox: simultaneous extracellular hyperglycemia and intracellular glucose deficiency. The consequences of this paradox are shown in Figures 1 and 2.<sup>4</sup>



## Clinical signs

There are three clinical scenarios in diabetes mellitus

- Uncomplicated
- Complicated by ketoacidosis
- Hyperosmolar hyperglycemic non-ketotic syndrome

### UNCOMPLICATED DIABETES MELLITUS

The classical signs are:

- Polyuria/Polydipsia
- Polyphagia
- Cachexia
- Increased susceptibility to infections (e.g. urinary tract and skin infections)



Complications, due to protein glycosylation, include

- Cataracts in dogs
- Peripheral neuropathy in cats

Fructosamine concentrations also increase due to protein glycosylation.

### COMPLICATED BY KETOACIDOSIS

Animals may become comatose if the ketoacidosis is severe.

### HYPEROSMOLAR HYPERGLYCEMIC NON-KETOTIC SYNDROME

When resistance of target tissues to insulin plays a role in the disease, insulin levels can be elevated. In these cases, ketosis is suppressed and blood glucose concentrations can become very high. These animals are usually comatose.

## Diagnosis

Diabetes mellitus is not the only cause of polyuria, polydipsia, polyphagia and weight loss. Cases should be investigated fully to rule out other causes before starting insulin treatment.<sup>5</sup> A preliminary diagnosis of diabetes mellitus based on clinical signs must be confirmed by urine and blood tests.

For reference intervals for blood glucose in non-diabetic, healthy animals, refer to your local or practice laboratory. The renal threshold is around 10 mmol/L (180 mg/dL) in dogs and around 14 mmol/L (252 mg/dL) in cats. If the blood glucose concentration exceeds this threshold, glucose is excreted in the urine (glucosuria).

Transient hyperglycemia can occur particularly in cats in stress situations, usually where struggling is involved. Fructosamine concentrations are correlated with the average blood glucose concentration over the previous 1-2 weeks. Fructosamine measurement is a valuable tool in confirming a diagnosis of diabetes mellitus particularly in cats.

## Diabetes management

### GENERAL CONSIDERATIONS

Treatment of diabetes mellitus is likely to succeed only if the pet owner understands all aspects of its management, including the importance of diet and regular exercise. Investment of time in a careful explanation of all aspects of diabetes management is strongly recommended.

### SPAYING

If diabetes mellitus has been diagnosed in an intact female dog, immediate spaying (ovariohysterectomy) is advisable, to prevent further exposure to endogenous progesterone. In animals fit for surgery, this can be carried out prior to insulin treatment and intravenous fluid therapy administered.

If the animal's condition is critical (dehydration, anorexia, uremia, severe hyperglycemia and glycosuria) and surgery is contraindicated, intravenous fluid therapy and insulin administration should be started. Spaying can then be carried out as soon as the dog's condition has improved sufficiently. On the day of surgery, pre-operative fasting will necessitate reducing the insulin dose, e.g. to around 30% and intravenous fluid therapy should be administered.

Following surgery, regular monitoring is necessary until the animal's condition is stable. The response to insulin will often improve and the insulin demand will decrease accordingly.

## Diet and feeding schedule

The volume and composition of meals should be identical from day to day to avoid changes in insulin requirements. As this is difficult to accomplish with home-prepared meals, commercial pet food is preferable.

Commercial diets with a high quality, highly digestible protein source and a low fat content provide a more gradual intestinal uptake of glucose. In animals that are over- or underweight, the ideal body weight should be reached by gradual weight loss or gain. Very calorie-dense diets, especially those high in soluble carbohydrates, should be avoided in animals that are underweight.

Clean drinking water should be available at all times. A reduction in excessive water consumption indicates successful management of the diabetes mellitus.



For diabetic dogs the daily food intake is usually divided into two meals. The first meal is usually fed around the time of the morning insulin injection and the second meal approximately 8 hours to 12 hours later. For dogs, diets that contain increased quantities of soluble and insoluble fiber or that are designed for weight maintenance or for weight loss if required are often recommended. These diets may help to improve glycemic control by reducing postprandial hyperglycemia and to restrict caloric intake in obese dogs undergoing weight reduction.<sup>3</sup>

Cats are often very fussy eaters and usually prefer to eat when they choose. Free access to a measured amount of the food is often the best option. Diabetic cats can be stabilized on their usual diet if need be, but diets with a high quality source of protein and low in carbohydrate are usually preferred.

If the cat is overweight, implement a weight management program to help reduce weight gradually. Weight loss will make the cat's diabetes easier to manage and is an important factor in cats that achieve remission.



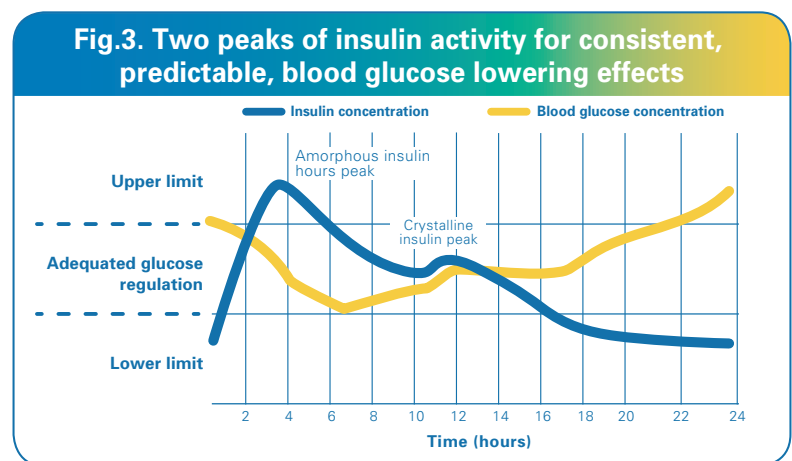
# Convenient Management of Diabetes with Caninsulin®

Due to differences in metabolism, the duration of activity of a particular insulin will vary from animal to animal. The source of the insulin can be also different. Caninsulin is an aqueous suspension of 40 IU highly purified porcine insulin per mL, consisting of 35% amorphous and 65% crystalline zinc insulin. Caninsulin is available in vials and it is administered using a U40 insulin syringe. Caninsulin offers a variety of options to optimize diabetes management and improve compliance.

## Proven efficacy in Dogs and Cats with Diabetes

### BENEFITS OF ONCE OR TWICE DAILY CANINSULIN IN DOGS

In dogs the amorphous fraction has peak activity approximately 4 hours after subcutaneous administration, and its effects last for about 8 hours.<sup>6</sup> This effect is maintained by the crystalline fraction, which has a slower onset of action and peak effects around 11 hours post-injection.<sup>6</sup> The total duration of effect ranges from 14 to 24 hours,<sup>7, 9, 10</sup> long enough for once daily administration in some cases. At least one-third of dogs adequately regulated using once-daily dosing (Figure 3).<sup>6-11</sup>



### BENEFITS OF TWICE DAILY CANINSULIN IN CATS

In cats, peak insulin activity is generally between 1.5 and 8 hours post-injection<sup>8,9</sup> and the total duration of action is around 12 hours.<sup>12</sup>

The duration of action of Caninsulin is shorter in cats than in dogs. As a result, all cats require twice daily injection. In the majority of diabetic cats, twice daily injection of Caninsulin provides good glycemic control and resolves the clinical signs of diabetes.<sup>12-15</sup>

## Presentations and Storage\*

- 40 IU/mL concentration for more accurate dosing in dogs and cats requiring <8 IU per injection
- Caninsulin is available in 10mL vials.
- Store upright and refrigerated, do not freeze

6. Graham PA et al. J Small Anim Pract. 1997;38:434-438. 7. Monroe WE et al. J Vet Intern Med. 2005;19:675-682. 8. Horn B, Mitten RW. Aust Vet J. 2000;78:831-834. 9. Davison LJ et al. Vet Rec. 2005;156:467-471. 10. Fleeman LM, Rand JS, Morton JM. Vet Rec. 2009;164:232-237. 11. Fracassi F et al. Vet Rec. 2018;183:262. 12. Martin GJ, Rand JS. J Feline Med Surg. 2001;3:23-30. 13. Michiels L et al. J Feline Med Surg. 2008;10:439-451. 14. Martin GJ, Rand JS. Vet Rec. 2007;161:88-94. 15. Zini E et al. J Vet Intern Med. 2010;24:1314-1321.



NOTE: Educate your client on the importance of using U40 insulin syringes.

## Initial Regulation\*

### DOGS

The initial dose for dogs is 0.5 - 1.0 IU/kg once daily. The dose per injection is often the same whether the insulin is administered once or twice daily. Consider changing to twice daily dosing if duration of insulin action is less than 14-16 hours after several weeks of treatment. Decrease once daily dose by 25% and administer as two equal doses at 12 hour intervals. For example, a dog on 20 IU once daily would receive an initial daily dose of 15 IU twice daily.

It is not uncommon for a dog's insulin requirements to change suddenly, even after a period of months or even years.

### CATS

The initial dose for cats is 1 to 2 IU per cat twice daily, depending on the initial blood glucose concentration (Figure 4). The starting dose should ideally not exceed 2 IU per cat twice daily in the first 3 weeks of treatment.

After several weeks or even months it is not unusual for either insulin to be no longer required (clinical remission) or a major change in the dose to be required.

Baseline blood glucose concentration	Initial Caninsulin dose (round down to nearest whole unit)
<20 mmol/l or <360 mg/dl	1 IU twice daily
≥20 mmol/l or ≥360 mg/dl	2 IU twice daily

Figure 4. Guide to starting twice Caninsulin treatment in cats

\* See package insert for full information.

## Dose adjustment

In dogs, dose adjustment should be managed in increments of 10%. In cats, the dose should be adjusted in increments of 0.5 to 1 IU.

After starting treatment or a dosage change, allow at least 7 days before assessing and making further changes (unless there is evidence of low blood glucose).

Maintaining a blood glucose concentration within the reference interval for nondiabetics throughout the entire day is not a treatment goal per se. The aim is to try to maintain blood glucose range of:

- **In dogs** >4.5-14 mmol/L or >81-252 mg/dL, for the majority of the day
- **In cats** >4.5-17 mmol/L or >81-300 mg/dL, for the majority of the day<sup>16</sup>

This will result in the disappearance of most of the clinical signs - a goal of therapy.

## Urine monitoring

Urine monitoring is a quick and easy method of detecting ketones (ketonuria).

Urine only tests positive for glucose if the blood glucose concentration remains above the renal threshold for a substantial period. Monitoring of urine for glucose can be useful in diabetic animals that are not yet stable or in those that have problems with recurrent hypoglycemia. Here it is used to identify the absence of glucose.

Urine monitoring can be used for animals that are known to have a blood glucose concentration in an acceptable range. In this case it is a quick, easy method of detecting hyperglycemia. This should then be investigated further by measuring blood glucose concentrations.

## Blood glucose curves

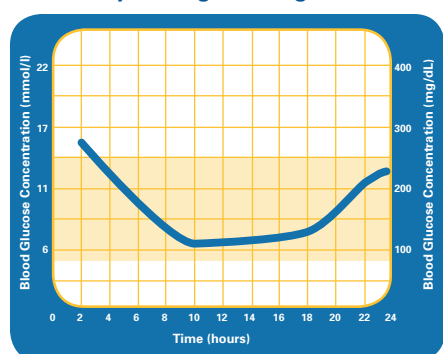
Blood glucose curves are a useful tool in the providing back-up information in diabetic dogs and cats to support the evolution of clinical signs during insulin treatment. They are vital in investigating poorly regulated and unstable diabetics.

The procedure is as follows:

- The dog or cat should be given his/her first meal before, during or after the Caninsulin injection by his/her morning Caninsulin injection
- Ideally, take the first blood sample just prior to the insulin administration. Blood samples should then be taken approximately every 2 hours throughout the day (at least 9 to 12 hours). It is important to record the time that the samples are taken. If blood glucose falls below 8.3 mmol/L or 150 mg/dL, consider checking hourly.

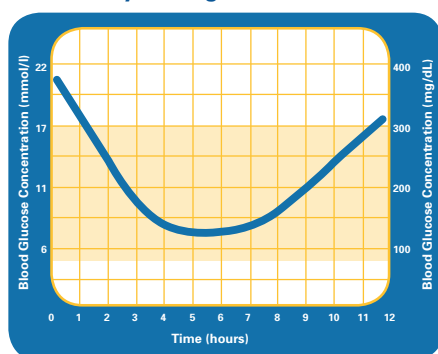
These charts show the curves you would expect to find in a diabetic dog and cat that have little or no clinical signs as well as 4 problem scenarios. Most of the examples below are plotted against over 24 hours but can be easily adapted to a 12-hour timeline. **NOTE:** Insulin given at time=0

### Ideal Blood Glucose Curve: Once Daily Dosing in a Dog



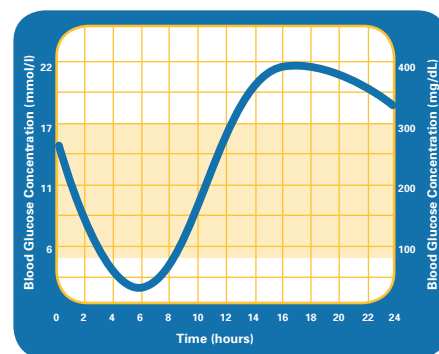
A stable diabetic dog maintains a blood glucose range of >4.5-14 mmol/L or >81-252 mg/dL for most of a 24-hour period. The renal threshold in the dog is 11-14 mmol/L or 200-252 mg/dL.

### Ideal 12-hour Blood Glucose Curve: Twice Daily Dosing in a Cat



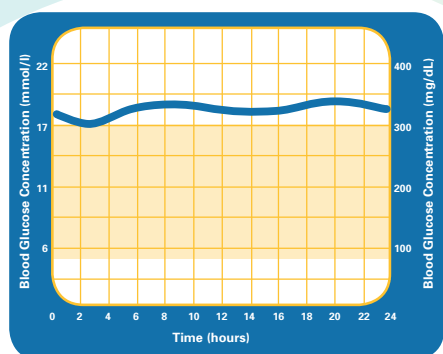
Ideally, the blood glucose should be >4.5-17 mmol/L or >81-300 mg/dL for the majority of the day.<sup>16</sup> The renal threshold in the cat is 14-17 mmol/L or 252-300 mg/dL.

### Glycemic instability



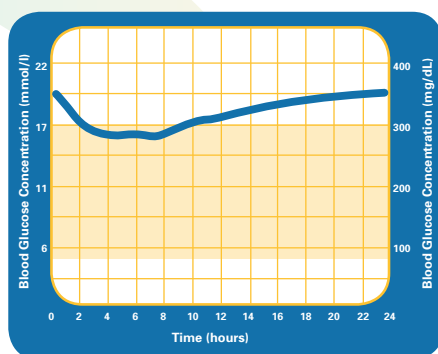
**Action:** If you document, see clinical signs of or suspect hypoglycemia (e.g. prolonged hyperglycemia in a previously responsive dog or cat): for dogs, decrease dose by 50% or more and for cats, decrease dose by 50% or return to starting dose of 1 or 2 IU/cat twice daily, whichever is lower. You may need to go back to the starting dose if the current dose is higher than 1.5-2.2 IU/kg.

### Insulin Resistance



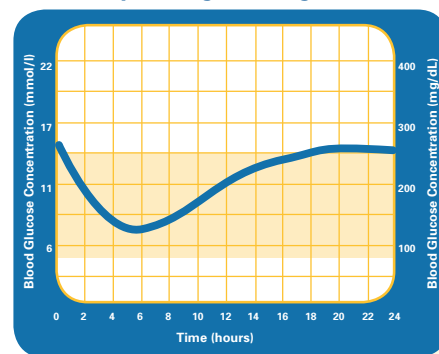
**Action:** Investigate cause, eg, concurrent disease, diabetogenic drugs, human factors, insulin storage and/or insulin dosing (see **Diagnostic Tests to Consider**). Consideration should be given to glycemic instability, which can present as persistent hyperglycemia or fluctuating blood glucose for a few days following the hypoglycemia (see **Glycemic instability**).

### Insufficient Insulin Dose



**Action:** Differentiate from insulin resistance and glycemic instability in dogs and cat and stress hyperglycemia in cats before carefully and gradually increasing the insulin dose.

### Short Duration of Insulin Action: Once Daily Dosing in a Dog



**Action:** If the duration of action is less than 14-16 hours, decrease once daily dose by 25% and administer this new dose twice daily.

**NOTE:** Cats need TWICE daily dosing.

## Problems with Regulation

If the response to insulin therapy is poor, a blood glucose curve should be made and every effort made to rule out other concurrent or underlying disorders.

Investigate and treat infection, predisposing and concurrent disorders before starting or adjusting insulin treatment:

- Medication (e.g. prednisolone or other corticosteroid, progestin)
- Obesity (in cats)
- Inflammation (e.g. gingivitis, pancreatitis)
- Infection (e.g. skin, urinary tract)
- Other endocrine disease:
  - dogs** - hyperadrenocorticism and hypothyroidism
  - cats** - acromegaly and hyperthyroidism
- Chronic kidney disease in cats



## Problems with Administration

Caninsulin has been specially developed for use in dogs and cats, and has a concentration of 40 IU/mL, making the dose easy to measure and dilution unnecessary. Caninsulin should be stored upright in a refrigerator and must be mixed before use. To obtain a homogeneous, uniformly milky suspension, mix thoroughly by shaking vials or inverting cartridges.

To avoid dosing errors when administering Caninsulin, it is important to use a U-40 insulin syringe.

## Problems with the injection site

Select an appropriate site for injection avoiding and alternate the injection site daily.

## Antibodies

The presence of antibodies is common in diabetic dogs and does not frequently lead to poor regulation. Antibody production is less likely in dogs if homologous insulin is given - the porcine insulin in Caninsulin has exactly the same structure as canine insulin. Insulin antibodies appear to be uncommon in diabetic cats.

## Management of Hypoglycemia

One of the most important complications seen in diabetic pets on insulin treatment is hypoglycemia.

If the blood sugar is too low, the brain does not receive enough glucose. Prepare pet owners to be aware of the situations in which this may occur and to watch out for these signs:

- Restlessness
- Trembling or shivering
- Unusual movements or behaviour
- Loss of consciousness (coma) and unusual quietness or sleepiness.

If these signs occur, it is important pet owners know what to do:

- Provide food immediately
- **If dog or cat refuses to eat or cannot eat**, administer a glucose source as quickly as possible. Always keep a ready source of glucose, for example glucose powder which can be mixed with tap water. Give one gram of glucose per kilogram body weight. Administer the solution very carefully. Make sure the solution does not go down the wrong way.
- **If dog or cat is unconscious or unable to swallow**, rub the glucose solution onto the gums and especially under the tongue. As soon as the dog or cat shows signs of recovery, take him/her to a veterinarian.

Advise your pet owners that, if dog or cat is unconscious or having a seizure - **this is an emergency!** They should contact you as soon as possible. The dog or cat will require hospitalization and intravenous fluids.



## Client participation

Most clients quickly learn to give daily insulin injections. It is best to confirm that the animal is eating normally, before giving the insulin injection.

During therapy the pet owner needs to actively participate in regularly monitoring their pet's progress.

Many clients can be successfully instructed to take capillary blood samples and use a handheld glucometer. If this is not feasible, an alternative is to have the owner test the urine for the presence of glucose and ketones. Before dose changes are made, blood glucose concentrations should be confirmed.

## Prognosis in diabetes mellitus

The prognosis for a diabetic pet depends to a large extent on the level of confidence, knowledge and dedication of his/her owner. These factors can be favorably influenced by your attitude and the quality of the information you, the veterinarian, provide.

It should be made clear that treating a diabetic pet is interesting, rewarding and certainly not as complicated as is sometimes thought.



## NAME OF THE VETERINARY MEDICINAL PRODUCT

Caninsulin 40 IU/ml Suspension for Injection

## QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Insulin\* 40 IU \*(Porcine insulin present as 35% amorphous Zinc insulin and 65% crystalline Zinc insulin).

## PHARMACEUTICAL FORM

A white to almost white suspension for injection.

## CLINICAL PARTICULARS

### Target Species

Dogs and cats

Indications for use, specifying the target species

Caninsulin is indicated in cases of diabetes mellitus (insulin deficiency) in dogs and cats, where the required blood glucose levels are achieved by using an individually adjusted dose of Caninsulin.

### Contraindications

Caninsulin is not intended for the treatment of animals with severe acute diabetes presenting in a ketoacidotic state. Caninsulin must not be administered by the intravenous route.

### Special warnings

None.

### Special precautions for use

#### Special precautions for use in animals

It is important to establish a strict feeding schedule in consultation with the owner which will include a minimum of fluctuations and changes. Clinical signs of hunger, increased anxiety, unstable locomotion, muscle twitching, stumbling or sinking in the rear legs and disorientation in the animal indicate hypoglycaemia and require immediate administration of glucose solution or food to restore blood glucose concentrations to normal.

The product must be administered with specific U-40 sterile single-use syringes (vial).

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Accidental self-injection can provoke clinical signs of hypoglycaemia, which should be treated by oral administration of glucose.

In case of accidental self-injection seek medical advice immediately and show the package insert or label to the physician

### Adverse reactions (frequency and seriousness)

Very rare cases of local adverse reactions associated with administration of porcine insulin have been reported in dogs and cats. These reactions are usually mild and reversible. In extreme rare cases, allergic reactions to porcine insulin have been reported.

### Use during pregnancy, lactation or lay

The use of Caninsulin is not contra-indicated during pregnancy or lactation but requires close veterinary supervision to account for changes in metabolic requirements during this period.

### Interaction with other medicinal products and other forms of interactions

Changes in insulin requirements may result from administration of substances which alter glucose tolerance such as corticosteroids and progestagens. Monitoring of glucose levels should be used to adjust dose accordingly. Similarly, changes in diet or exercise routines may alter insulin requirements.

### Amounts to be administered and administration route

Caninsulin should be administered once or twice daily, as appropriate, by subcutaneous injection. Shake the vial thoroughly until a homogeneous, uniformly milky suspension is obtained. Foam on the surface of the suspension formed during shaking should be allowed to

disperse before the product is used and, if required, the product should be gently mixed to maintain a homogeneous, uniformly milky suspension before use. Agglomerates can form in insulin suspensions. Do not use the product if visible agglomerates persist after shaking thoroughly.

When using vials:

A 40 IU/ml insulin syringe should be used.

When using product in cartridges:

The cartridge is designed to be used with a VetPen. VetPen is accompanied by package leaflet with detailed instruction for use to be followed.

### Stabilisation phase

Dog: Insulin therapy is initiated with the starting dose of 0.5 IU/kg bodyweight once daily, rounded down to the lowest entire number of units. Some examples are given in the following table.

Dog body weight Starting dose per dog

5kg	2IU once daily
10kg	5IU once daily
15kg	7IU once daily
20kg	10IU once daily

Subsequent adjustment to establish the maintenance dose should be made by increasing or decreasing the daily dose by approximately 10% according to the evolution of the diabetes clinical signs and to the results of serial blood glucose measurement. Alterations in dose should not normally be made more frequently than every 3 to 7 days. In some dogs, the duration of insulin action may require treatment to be administered twice daily. In such cases, the dose per injection must be decreased by 25% so that the total daily dose is less than doubled.

For example, for a 10 kg dog receiving 5 IU once daily, the new dose (rounded down to the nearest whole unit) would be 3 IU per injection initially. The two daily doses should be administered at 12h intervals. Further dose adjustments should be made progressively as previously explained.

To achieve a balance between the generation of glucose and the effect of the product, feeding should be synchronized with the treatment and the daily ration divided into two meals. The composition and quantity of the daily food intake should be constant. In dogs treated once daily, the second meal is usually fed at the time of peak insulin effect.

In dogs treated twice daily, feeding coincides with Caninsulin administration. Each meal should be fed at the same time each day.

Cat: The initial dose is 1 IU or 2 IU/kg per injection based on the baseline blood glucose concentration, as presented in the following table.

### Cats require twice daily administration.

Cat blood glucose concentration

<20 mmol/l or <3.6 g/l (<360 mg/dl)	Starting dose per cat 1 IU twice daily
≥20 mmol/l or ≥ 3.6 g/l (≥360 mg/dl)	2 IU twice daily

The composition and quantity of the daily food intake should be constant.

Subsequent adjustment to establish the maintenance dose should be made by increasing or decreasing the daily dose according to the results of serial blood glucose measurement. Alterations in dose should not normally be made more frequently than every week. Increments of 1 IU per injection are recommended. Ideally, no more than 2 IU should be administered per injection in the first three weeks of treatment. Due to the day-to-day variation in the blood glucose response, and the variations in insulin responsiveness that are seen with time, larger or more frequent increases in dose are not recommended.

### Maintenance phase in dogs and cats

Once the maintenance dose has been reached and the animal is stabilised, a long-term management programme needs to be established. The aim should be to manage the animal in such a way as to minimise the variations in its insulin requirement. This includes clinical monitoring to detect under or overdosage of insulin and adjustment of dose if required. Careful stabilisation and monitoring will help to limit the chronic problems associated with diabetes, including cataracts (dogs), fatty liver (dogs and cats), etc.

Follow up examinations should be performed every 2-4 months (or more often if there are problems) to monitor the animal's health, the owner's records, urine glucose and biochemical parameters (like blood glucose and/or fructosamine concentration). Adjustments to the insulin dose should be made based on

interpretation of the clinical signs supported by the laboratory results.

### Overdose

Overdose of insulin results in clinical signs of hypoglycaemia. Owners and veterinarians should be aware of the Somogyi over-swing which is a physiological response to hypoglycaemia. As a partial hypoglycaemia begins to develop a hormonal response is triggered which results in the release of glucose from hepatic glycogen stores. This results in rebound hyperglycaemia, which may also manifest as glucosuria for part of the 24-hour cycle. There is a danger that the Somogyi over-swing will be interpreted as a requirement for an increase in the insulin dose rather than a decrease. This situation can progress to an overdose so large as to cause clinical hypoglycaemic effects.

### Pharmacodynamic properties

Insulin facilitates the uptake of glucose by cells and activates intracellular enzymes involved in the use and storage of glucose, amino acids and fatty acids. Insulin also inhibits catabolic processes such as proteolysis, gluconeogenesis and lipolysis. Diabetes mellitus is characterised by an absolute or relative insulin deficiency leading to persistent hyperglycaemia, and monitoring blood glucose concentration enables assessment of the overall effect of the administered insulin. In diabetic dogs, the action of Caninsulin on blood glucose concentrations, following subcutaneous administration, peaks at about 6-8 hours post-injection and lasts for about 14 to 24 hours. In diabetic cats, the action of Caninsulin on blood glucose concentrations after subcutaneous administration peaks at about 4-6 hours and last for about 8 to 12 hours post-injection.

### Pharmacokinetic particulars

Caninsulin is an insulin of intermediate duration of action that contains both amorphous and crystalline insulin in a 3.5:6.5 ratio. In diabetic dogs, the peak plasma concentration of insulin occurs at about 2-6 hours after subcutaneous injection, and insulin remains above pre-injection level for about 14 to 24 hours. In diabetic cats, the peak plasma concentration of insulin occurs at about 1.5 hours after subcutaneous injection and insulin remains above pre-injection level for about 5 to 12 hours.

### Incompatibilities

None known.

### Shelf-life

Shelf life: 2 years. Vials: following withdrawal of the first dose, use the product within 42 days. Cartridges: following withdrawal of the first dose, use the product within 28 days.

### Special precautions for storage

Store upright and refrigerated between +2 C and +8 C.

Do not freeze

Protect from light.

After first opening, store below 25°C and away from direct heat or direct light.

### Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Any unused product or waste material should be disposed of in accordance with national requirements.

Distributed by: Intervet International BV, PO Box 31, 5830AA Boxmeer, The Netherlands.



## The FIRST veterinary insulin approved for BOTH dogs and cats

- Global leader in veterinary diabetes care
- Tried and trusted in the field
- The first choice insulin for dogs<sup>3,17</sup> suitable for once or twice daily administration
- A good choice for cats suitable for twice daily administration and with comparable remission rates to other commonly used insulins<sup>15,18</sup>
- Flexible options for easy dosing to suit all sizes
- Experience and professional support from the global market leader

### Take advantage of useful resources for your clinic and pet owners:

- [www.caninsulin.com](http://www.caninsulin.com) for your clinic
- [www.pet-diabetes.com](http://www.pet-diabetes.com) for pet owners
- Training Videos and Materials
- Glucose Curve Worksheets
- Pet Diabetes Tracker App
- Sugar and Spike resources



**For general information and pet diabetes management tools, please visit [www.caninsulin.com](http://www.caninsulin.com) or ask your MSD Animal Health Representative today**

3. Behrend E et al. J Am Anim Hosp Assoc. 2018; 54:1–21.  
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