
Pet Owner

Pet's Name

Curve Kit

Glucose Curve Workpad

How-to Instructions

Interpretation Guidelines

Stabilisation Protocol

SAMPLING FOR GLUCOSE CURVES

ADMISSION:

Admit the dog or cat first thing before eating and receiving Caninsulin® or immediately after eating and receiving Caninsulin at home. Be sure to ask the owner how their pet is getting on and review any records they keep at drop-off. After admission, it's important that the dog or cat keeps to the same meal and exercise routine as at home. Body weight should be measured and recorded.

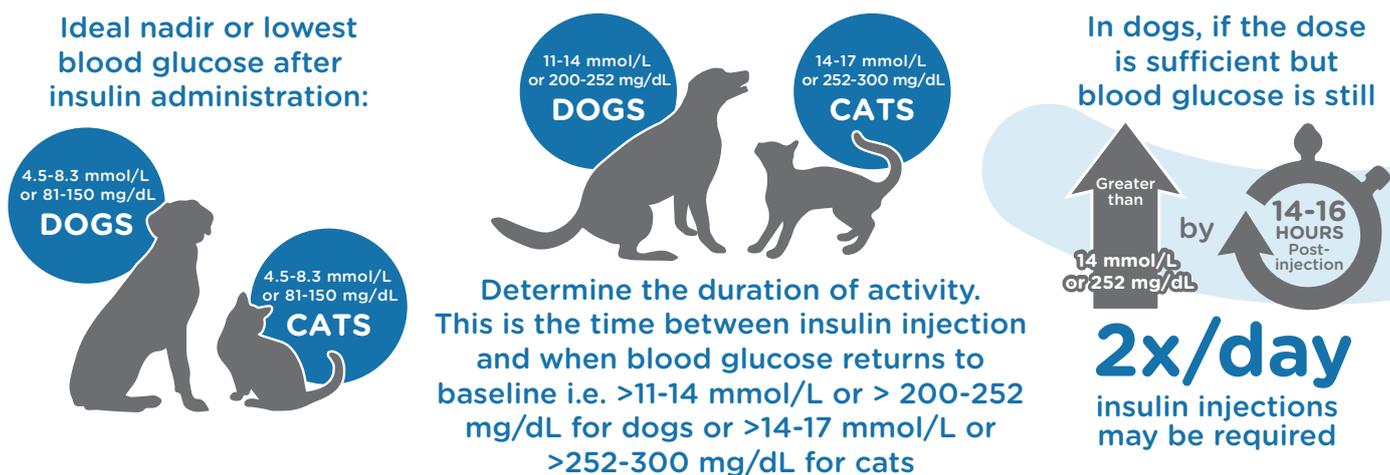
BLOOD SAMPLING:

Measure blood glucose at least every 2 hours. Ideally, continue for 9-12 hours. If blood glucose falls below 8.3 mmol/L or 150 mg/dL, consider checking hourly.¹

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).

CHART:

Plot the blood glucose concentrations against time. Look at the pattern of the values before connecting with lines. Remember that there is considerable variation in insulin curves between days even in an individual dog or cat.



NOTE: Capillary blood samples can be taken from the lateral ear margin in cats or lip fold in dogs. Alternative sites include the pisiform pad or elbow callus. To minimize variability either capillary or venous samples should be taken.

INTERPRETING GLUCOSE CURVES

Evaluate the glucose curve and compare it to the charts below before revising your treatment plan.

Serial 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.

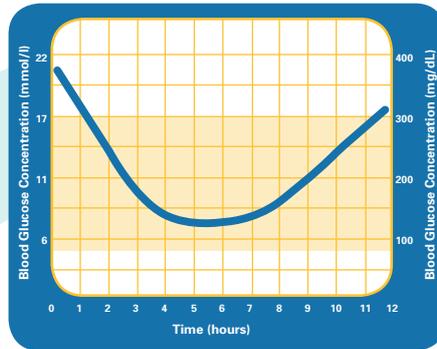
These charts show the curves you would expect to find in a diabetic dog and cat that have little or no clinical signs as well as 4 problem scenarios. Most of the examples below are plotted against over 24 hours but can be easily adapted to a 12-hour timeline. **NOTE:** Insulin given at time=0

Ideal Blood Glucose Curve: Once Daily Dosing in a Dog



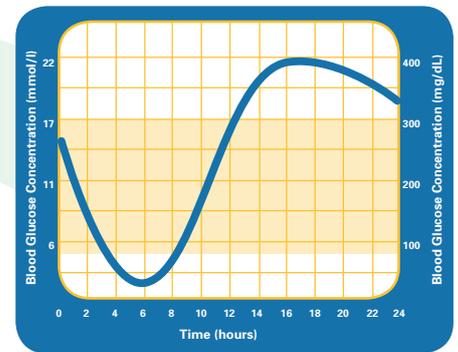
A stable diabetic dog maintains a blood glucose range of >4.5-14 mmol/L or >81-252 mg/dL for most of a 24-hour period. The renal threshold in the dog is 11-14 mmol/L or 200-252 mg/dL.

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.² The renal threshold in the cat is 14-17 mmol/L or 252-300 mg/dL.

Glycemic instability



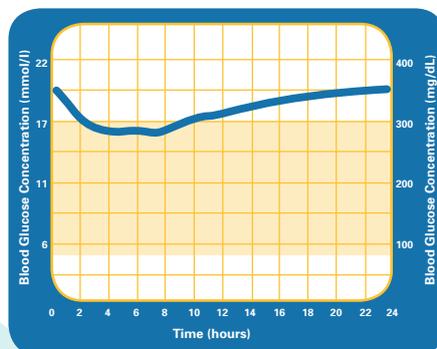
Action: If you document, see clinical signs of or suspect hypoglycemia (e.g. prolonged hyperglycemia in a previously responsive dog or cat): for dogs, decrease dose by 50% or return to starting dose of 1 or 2 IU/cat twice daily, whichever is lower. You may need to go back to the starting dose if the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

FACTORS AFFECTING INSULIN EFFECTIVENESS

Several diabetogenic drugs (such as glucocorticoids, progestins, amitraz, medetomidine, dexmedetomidine, xylazine and progestins) and concurrent disorders can affect blood glucose in dogs and cats and interfere with the effectiveness of insulin therapy. Some concurrent disorders (such as skin, ear and urinary tract infections) can be detected easily. However, others may require extensive diagnostic testing. It is advisable to rule out concurrent disease prior to starting insulin treatment as well as if there are any changes in insulin effectiveness.

DIAGNOSTIC TESTS TO CONSIDER¹

- Complete blood count (CBC), serum biochemistry panel, including triglyceride, amylase and lipase urinalysis (including urine specific gravity (refractometer))
- Bacterial culture of the urine
- Pancreas specific lipase (dog/cat) (pancreatitis)
- Serum trypsin-like immunoreactivity (exocrine pancreatic insufficiency, pancreatitis)



DIAGNOSTIC IMAGING

- Abdominal ultrasonography (adrenomegaly, adrenal mass, pancreatitis, pancreatic mass)
- Thoracic radiography (cardiomegaly, neoplasia)
- MRI (pituitary mass)

ENDOCRINE TESTS

- Adrenocortical function tests
 - ACTH stimulation test (hyperadrenocorticism)
 - Low-dose dexamethasone suppression test (hyperadrenocorticism)
- Thyroid function tests
 - Baseline serum total and free T₄ (hypothyroidism or hyperthyroidism)
 - Endogenous TSH (hypothyroidism)
- Serum progesterone (diestrus in intact female dog)
- Plasma growth hormone or serum insulin-like growth factor I (acromegaly)



REFERENCES:

1. Feldman EC, Nelson RW. Diagnostic tests to consider for the evaluation of insulin resistance in diabetic dogs and cats. In. Canine and Feline Endocrinology and Reproduction, 3rd ed. St. Louis, MO: Saunders; 2004. p. 526.
2. Feldman EC. Diabetes remission in cats: which insulin is best? Compend Contin Educ Vet. 2009;31(7 Suppl A).

QUESTIONS? WE'RE HERE FOR YOU.

For support and answers from MSD Animal Health diabetes professionals, visit www.caninsulin.com or contact us via our page www.msd-animal-health-me.com/company/contact-us/

GIVING INSULIN TO YOUR PET

Injections tips

- If necessary, ask someone to hold your pet prior to injecting Caninsulin.
- Ideally, the site of injection should be rotated from behind shoulder blade to slightly in front of hip bone and alternated between left and right sides. Ask your veterinarian for advice.
- Feed your pet before, during and after the injection, based on your vet's advice.

- Caninsulin should be stored upright in the fridge. Do not freeze.
- Shake the vial thoroughly to obtain a homogeneous, uniformly milky suspension.
- Carefully remove the cap from the U40 insulin syringe needle and insert the needle into the Caninsulin vial.
- Draw up the correct dose of Caninsulin into the U40 insulin syringe (1).
- Before injection, remove air bubbles by tapping the U40 insulin syringe with your finger and then pressing the plunger very gently (1).
- Draw the skin gently upwards and make a small hollow with your index finger (2).
- Place the needle in this hollow and push it gently through the skin (3) and then release the skin.
- Depress the syringe plunger steadily until all of the insulin dose has been injected.



IMPORTANT:

Only use a U40 insulin syringe with Caninsulin.

* See package insert for full information.

STABILISATION



Stabilisation phase when first commencing Caninsulin® treatment

Starting dose of 0.5 to 1 IU/kg* bodyweight SID.

Example: a 10.5 kg dog with a blood glucose concentration of 26 mmol/l starting on 0.5 IU/kg will get 5 IU ($10 \times 0.5 = 5$ IU) rounded down to the lowest entire number of units).

Dose adjustments in dogs

- Wait at least five to seven days before any dose adjustment is made.
- Adjustments to the insulin dose should be made based on interpretation of the clinical signs and supported by a blood glucose curve (BGC) with fructosamine (See “Interpreting Glucose Curves”).
- If the glucose curve shows a short duration of action, adjust the dose to twice daily (BID).
 - When adjusting to twice daily dosing give 75% of the original dose at each injection so that the total daily dose is less than doubled.
 - **Example:** a 10 kg dog receiving 5 IU once daily the new dose per injection twice daily is 75% of 5 (i.e. 3.75) rounded down to the nearest whole unit would be 3 IU per injection initially.

TOP TIPS

- The dog’s body weight should be rounded down to the nearest whole kilogram.
- The calculated dose of insulin should be rounded down to the nearest whole or half unit.

Starting on twice daily insulin dosing

- If the dog is beginning twice daily dosing from the initial outset, rather than once daily then the starting insulin dose in this case is selected based on the blood glucose concentration:

Blood glucose concentration	Starting insulin dose
<20 mmol/l or <3.6 g/l (<360 mg/dl)	0.25IU/kg
>20 mmol/l or 3.6 g/l (360 mg/dl)	0.5IU/kg

- The two daily doses should be administered at 12-hour intervals.
- The dose should only ever be adjusted by 10% up or down according to both the evolution of the clinical signs of diabetes mellitus and to the results of serial blood glucose measurement.
- **Example:** if dog is on 10 IU BID and insulin needs to be increased: 10% of 10 is 1, therefore give 11 IU am and 11 IU pm.
 - If Blood Glucose (BG) is <5 mmol/l at any time decrease dose by 10%. Re-curve the next day and daily thereafter until a nadir >5 mmol/l is reached..

Feeding

Once daily dosing: Feed half the daily meal at time of insulin injection and feed other half at peak insulin activity, which occurs in dogs between 4-8 hours post subcutaneous injection.

Twice daily dosing: Feed half the daily meal to coincide with the first injection and the other half of the meal with the subsequent injection (12 hours later).

Long-term management once stable

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, blood glucose and/or fructosamine concentration and urine glucose.

STABILISATION



Cats

Stabilisation phase when first commencing Caninsulin[®] treatment

- The initial dose is 0.25 IU/kg or 0.5 IU/kg per injection based on the baseline blood glucose (BG) concentration, as presented in the following table:

Cat blood glucose concentration	Starting dose per cat
<20 mmol/l or <3.6 g/l (<360 mg/dl)	0.25 IU/kg twice daily (up to a maximum of 2 IU per injection)
≥20 mmol/l or 3.6 g/l (360 mg/dl)	0.5 IU/kg twice daily (up to a maximum of 2 IU per injection)

- Cats require twice daily administration.

- **Examples:**

a 4.5 kg cat with a blood glucose concentration of 18 mmol/l will require a starting dose of 1 IU per injection. ($4 \times 0.25 = 1$ IU when weight is rounded down to the nearest whole kg).

a 4.5 kg cat with a blood glucose concentration of 22 mmol/l will require a starting dose of 2 IU per injection ($4 \times 0.5 = 2$ IU. The starting dose should not exceed 2 IU per injection.)

Dose adjustments in cats

- Adjustments to the insulin dose should be made based on interpretation of the clinical signs and supported by a blood glucose curve (BGC) with fructosamine. (See “Interpreting Glucose Curves”).
- Ideally, no more than 2 IU should be administered per injection in the first three weeks of treatment.
- Alterations in dose should not normally be made more frequently than every week.
- Increments of 1 IU per injection are recommended. However, if BG is <5 mmol/l at any time decrease the dose by 0.5 - 1 IU. Re-curve the next day and daily thereafter until a nadir >5 mmol/l is reached.

Feeding

Allow cats to eat as they are accustomed, accounting for their clinical condition.

Long-term management once stable

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, blood glucose and/or fructosamine concentration and urine glucose.

*To reduce the risk of hypoglycaemia, it is recommended to administer as low a dose as required within the starting dose range.

Caninsulin[®] 40 IU/ml Suspension for Injection contains porcine insulin, present as 35% amorphous Zinc insulin and 65% crystalline Zinc insulin, as active ingredient and is indicated in cases of diabetes mellitus (insulin deficiency) in dogs and cats.

Use medicines responsibly.

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GLUCOSE CURVE WORKSHEET



Date: _____ Pet Owner's name: _____

Pet's Name: _____

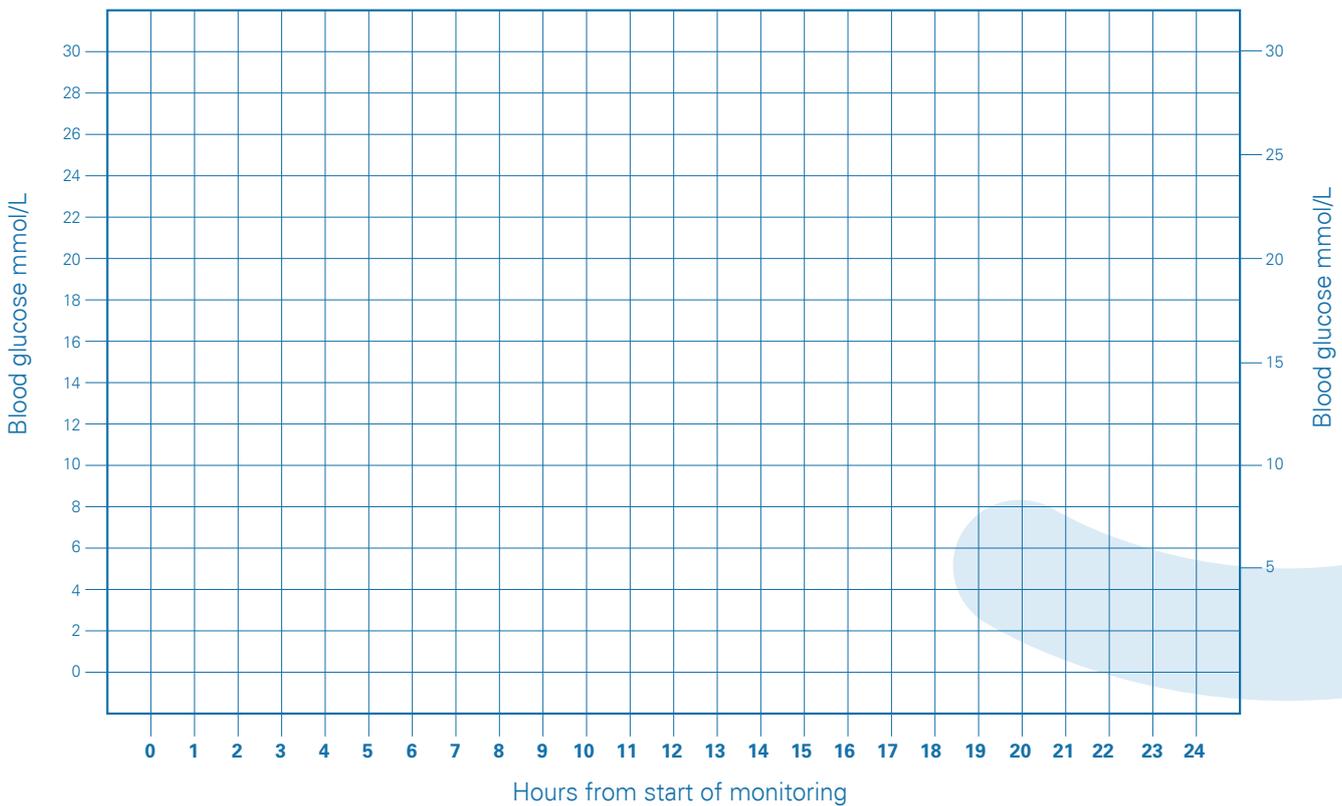
Age: _____ Sex: _____ Weight: _____ Neutered (please select one): Yes No

Breed: _____ Feeding time: _____

Body condition (please select one)*: 1 2 3 4 5

*1 = very thin, 2 = underweight, 3 = ideal weight, 4 = overweight, 5 = obese (score out of 5)

Please record time of injection(s) on the chart



Time of 1st meal: _____

Time of 2nd meal: _____

Units of Caninsulin® Administered: _____ IU

Units of Caninsulin® Administered: _____ IU

Time of 1st Insulin administration: _____ h _____ min

Time of 2nd Insulin administration: _____ h _____ min

Time Glucose Curve started: _____ h _____ min

Comments: _____

*Make sure to return this paper to your vet as soon as possible.

Caninsulin® should not be used in dogs or cats known to have a systemic allergy to pork or pork products. Caninsulin® is contraindicated during periods of hypoglycemia. Keep out of reach of children. As with all insulin products, careful patient monitoring for hypoglycemia and hyperglycemia is essential to attain and maintain adequate glycemic control and prevent associated complications. Overdosage can result in profound hypoglycemia and death. The safety and effectiveness of Caninsulin® in puppies and kittens, breeding, pregnant, and lactating dogs and cats has not been evaluated. See package insert for full information regarding contraindications, warnings, and precautions.

*Caninsulin is known as Vetsulin® in the U.S.A.

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GLUCOSE CURVE WORKSHEET



Date: _____ Pet Owner's name: _____

Pet's Name: _____

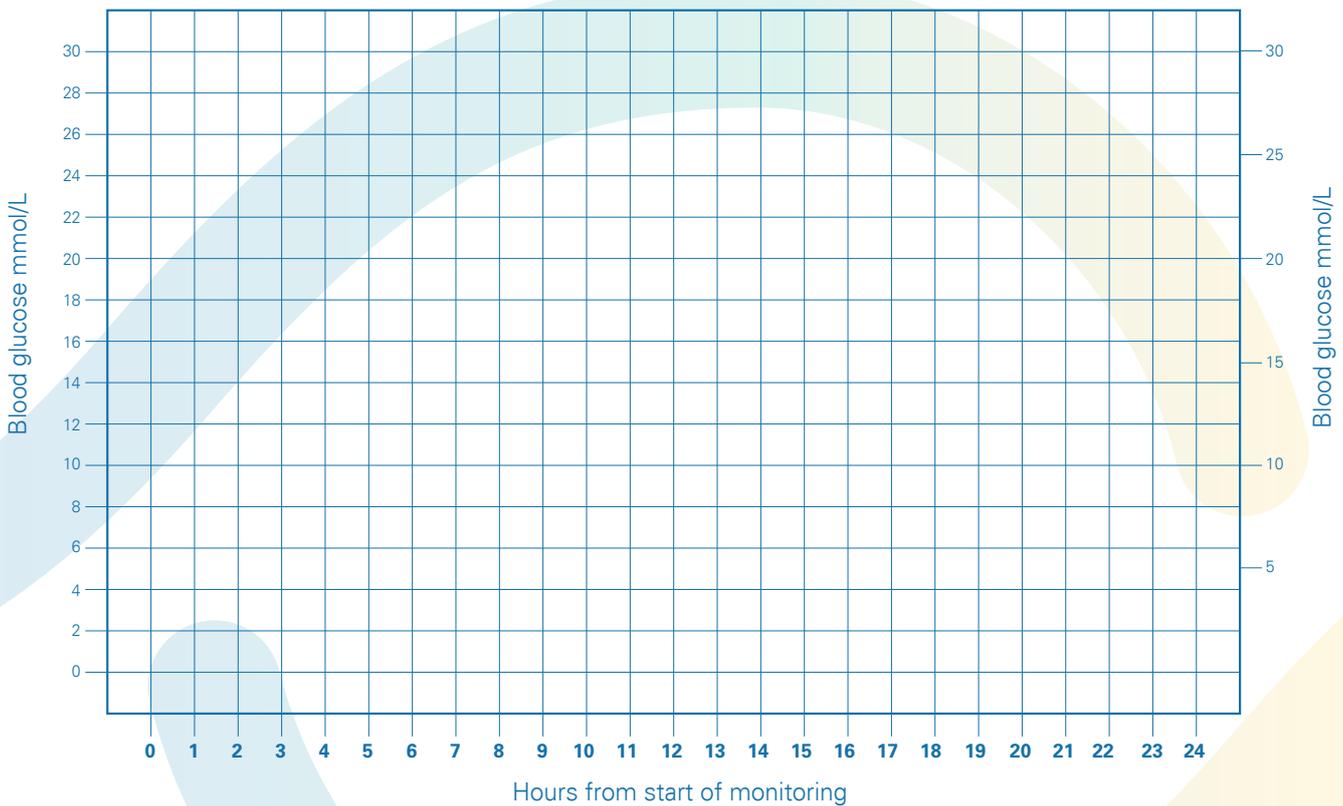
Age: _____ Sex: _____ Weight: _____ Neutered (please select one): Yes No

Breed: _____ Feeding time: _____

Body condition (please select one)*: 1 2 3 4 5

*1 = very thin, 2 = underweight, 3 = ideal weight, 4 = overweight, 5 = obese (score out of 5)

Please record time of injection(s) on the chart



Time of 1st meal: _____ Time of 2nd meal: _____

Units of Caninsulin® Administered: _____ IU Units of Caninsulin® Administered: _____ IU

Time of 1st Insulin administration: _____ h _____ min Time of 2nd Insulin administration: _____ h _____ min

Time Glucose Curve started: _____ h _____ min

Comments: _____

*Make sure to return this paper to your vet as soon as possible.

Caninsulin® should not be used in dogs or cats known to have a systemic allergy to pork or pork products. Caninsulin® is contraindicated during periods of hypoglycemia. Keep out of reach of children. As with all insulin products, careful patient monitoring for hypoglycemia and hyperglycemia is essential to attain and maintain adequate glycemic control and prevent associated complications. Overdosage can result in profound hypoglycemia and death. The safety and effectiveness of Caninsulin® in puppies and kittens, breeding, pregnant, and lactating dogs and cats has not been evaluated. See package insert for full information regarding contraindications, warnings, and precautions.

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

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 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 to 1 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 Starting dose per cat

<20 mmol/l or <3.6 g/l (<360 mg/dl) 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.

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caninsulin®

with you for life

Take advantage of useful pet diabetes management and support tools for your clinic and pet owners

- www.caninsulin.com for your clinic
- www.pet-diabetes.com for pet owners
- Training Videos and Material
- Glucose Curve Worksheets and more.



In case you suspect an adverse event associated with the usage of **Caninsulin**, please report immediately to **AH-Pharmacovigilance-ME@merck.com**.

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