

Managing Canine and Feline Patients with Diabetes Mellitus



MANAGING CANINE PATIENTS WITH DIABETES MELLITUS

CONFIRM DIAGNOSIS

- Confirm diagnosis glucosuria, chronic hyperglycemia (>15 mmol/L or 270 mg/dL)
- Investigate and treat infection, predisposing and concurrent disorders before starting or adjusting insulin treatment or if problems occur
- Spay intact female dogs

MANAGE DIABETES - Insulin and Diet

- 0.5-1 IU/kg Caninsulin[®] once daily
- Educate the client on the importance of using U40 insulin syringes or VetPen®, an insulin pen, and a new needle for each injection
- Change the dose in increments of 10% per injection
- Feed a suitable diet twice daily or ad libitum. Advise on suitable treats
- Ensure fresh drinking water is always available
- Schedule follow-up visits every 1-3 weeks:
- Weigh the dog. Ask if the dog is happy / hungry / thirsty / eating well / urinating frequently? How is the owner getting on? Have there been any changes since the last visit?
- Schedule examinations more frequently if there is something wrong (e.g. suspicion or evidence of hypoglycemia)
- 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
- Schedule follow-up examinations every 2-4 months. Dose adjustments may still be required from time to time

IF PROBLEMS DEVELOP OR SIGNS RECUR

Observe owner preparing and giving injection using their own supplies

Dosage regimen	Twice daily? On this dose for 1-3 weeks or more? >2.0 IU/kg?
Storage	Upright in the fridge? Correct storage temperature? Between doses? Not frozen? Product dating? In use for more than 28 days? Stored in the original container? Diluted?
User	Mixing insulin properly? Using same syringe/needle repeatedly? Is VetPen working properly? Selecting correct dose? Suitable injection site? Correct injection technique

INVESTIGATE AND TREAT INFECTION, PREDISPOSING AND CONCURRENT DISORDERS

- History of Medication (e.g. prednisolone or other corticosteroid, progestin)
- Inflammation (e.g. gingivitis, pancreatitis)

FURTHER INVESTIGATE USING CLINICAL SIGNS AND 8-12 EVENLY SPACED BLOOD GLUCOSE MEASUREMENTS



	Owner reports dog is	Blood glucose	Action
	Not happy. No better or drinking and urinating more	 Mainly >14 mmol/L (>252 mg/dL) Nadir >8.3 mmol/L (>150 mg/dL) or not present 	 Investigate predisposing and concurrent disorders Decrease dose by 25% and consider twice daily dosing (of this dose) Follow-up in 1 week
	Quiet, drowsy, weak, cold/shivering OR drinking and urinating more	 Mainly >14 mmol/L (>252 mg/dL) Nadir <4.5 mmol/L (<81 mg/dl) confirmed or suspected at any time 	 Decrease dose by 25% OR to dose at last visit (if signs have returned since then) Consider twice daily dosing (reduce dose by 25% and administer twice daily) Follow-up in 1 week
	Happy. Doing well. Showing few/no clinical signs	• Mainly >14 mmol/L (>252 mg/dL)	Investigate predisposing and concurrent disorders

- Infection (e.g. skin, urinary tract)
- Other endocrine disease (hyperadrenocorticism, hypothyroidism)

- Mainly 4.5-14 mmol/L (81-252 mg/dL) • Nadir 4.5-8.3 mmol/L (81-150 mg/dL)
- Stay on current dose
- Recheck every 2-4 months (sooner if clinical signs return)

MANAGING FELINE PATIENTS WITH DIABETES MELLITUS

CONFIRM DIAGNOSIS

- Confirm diagnosis glucosuria, chronic hyperglycemia (>15 mmol/L or 270 mg/dL) and fructosamine >380 µmol/L
- Investigate and treat infection, predisposing and concurrent disorders before starting or adjusting insulin treatment or if problems occur

MANAGE DIABETES - Insulin and Diet

- 1 to 2 IU Caninsulin® per cat twice daily
- Educate the client on the importance of using U40 insulin syringes or VetPen[®], an insulin pen, and a new needle for each injection
- Change the dose in increments of 0.5 or 1 IU per injection
- Do not exceed 2 IU per injection in the first 3 weeks of treatment
- Feed a suitable diet twice daily or ad libitum. Advise on suitable treats
- Ensure fresh drinking water is always available
- Schedule follow-up visits every 1-3 weeks:
- Weigh the cat. Ask if the cat is happy / hungry / thirsty / eating well / urinating frequently? How is the owner getting on? Have there been any changes since the last visit?
- Schedule examinations more frequently if there is something wrong (e.g. suspicion or evidence of hypoglycemia)
- Continue to adjust the insulin dose gradually (0.5 or 1 IU increase per injection every 1-3 weeks, if needed) until the clinical signs have improved or resolved
- Schedule follow-up examinations every 2-4 months. Dose adjustments may still be required from time to time

IF PROBLEMS DEVELOP OR SIGNS RECUR

Observe owner preparing and giving injection using their own supplies

Dosage regimen	Twice daily? On this dose for 1-3 weeks or more? >1.5 IU/kg?
Storage	Upright in the fridge? Correct storage temperature? Between doses? Not frozen? Product dating? In use for more than 28 days? Stored in the original container? Diluted?
User	Mixing insulin properly? Using same syringe/needle repeatedly? Is VetPen working properly? Selecting correct dose? Suitable injection site? Correct injection technique

INVESTIGATE AND TREAT INFECTION, PREDISPOSING AND CONCURRENT DISORDERS

- History of Medication (e.g. prednisolone or other corticosteroid, progestin)
- Obesity
- Inflammation (e.g. gingivitis, pancreatitis)

FURTHER INVESTIGATE USING CLINICAL SIGNS AND 8-12 EVENLY SPACED BLOOD GLUCOSE MEASUREMENTS





- Infection (e.g. skin, urinary tract)
- Other endocrine disease (acromegaly, hyperthyroidism)
- Chronic kidney disease

• Mainly 4.5-17 mmol/L (81-300 mg/dL) • Nadir 4.5-8.3 mmol/L (81-150 mg/dL)

- Stay on current dose
- Recheck every 2-4 months (sooner if clinical signs return)

Action • Investigate predisposing and concurrent disorders • Decrease dose to 1 or 2 IU twice daily if twice daily dose is ≥2 IU OR >1.5 IU/kg OR to dose at last visit (if signs have returned since then)

- Follow-up in 1 week
- Decrease dose to 1 or 2 IU twice daily if twice daily dose is ≥ 2 IU OR >1.5 IU/kg OR to dose at last visit (if signs have returned since then)
- Follow-up in 1 week

	• Is the cat stressed?
/	Investigate predisposing and concurrent disorders
	Stop insulin

- Recheck blood glucose after 12-24 hours without insulin
- Maintain cat on suitable diet

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/1 or <3.6 g/l (<360 mg/dl) 1 IU twice daily

 \geq 20 mmol/l or \geq 3.6 g/l (\geq 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

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 Special precautions for the disposal of unused veterinary medicinal from hepatic glycogen stores. This results in rebound hyperglycaemia, which may products or waste materials derived from the use of such products also manifest as glucosuria for part of the 24-hour cycle. There is a danger that Any unused product or waste material should be disposed of in accordance with the Somogyi over-swing will be interpreted as a requirement for an increase in national requirements. 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.

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



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
- Pet Diabetes Tracker App
- Sugar & Spike resources

For general information and pet diabetes management tools, please visit www.caninsulin.com or ask your MSD Animal Health Representative today

References:

- 1. Feldman EC, Nelson RW. In. Canine and Feline Endocrinology and Reproduction, 3rd ed. St. Louis, MO: Saunders; 2004. p. 526.
- 2. Feldman EC. Compend Contin Educ Vet. 2009;31(7 Suppl A).
- 3. Sparkes AH et al. 2015;17:235-250
- 4. Behrend E et al. J Am Anim Hosp Assoc. 2018; 54:1-21
- 5. Ackerman N et al. Companion Animal. 2018;23:143-151.