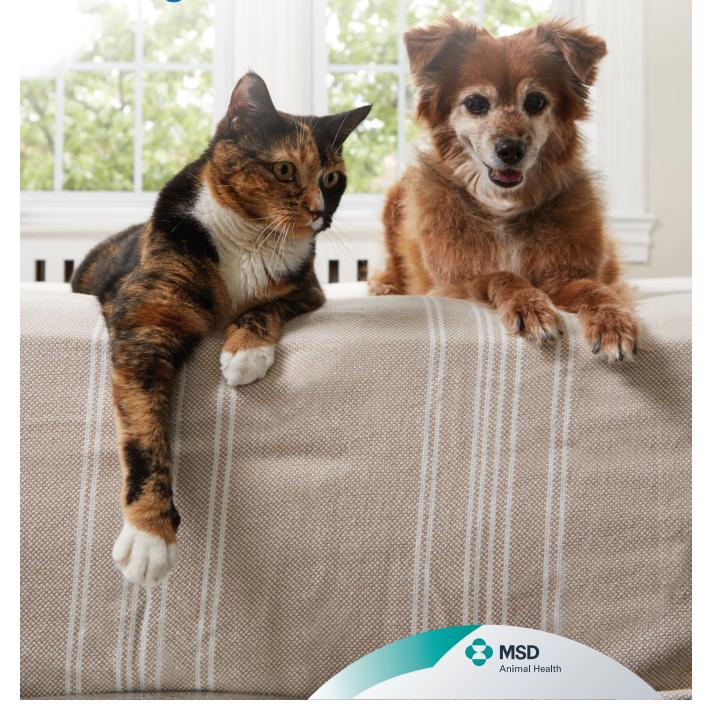


Management of Diabetes Mellitus in Dogs and Cats





With you for life... Convenient management of diabetes with Caninsulin®

The goals in managing Diabetes mellitus in dogs and cats are to reduce or eliminate the clinical signs of diabetes and minimize the risk of hypoglycemia. Remission is a goal that can be achieved in some diabetic cats. Dog and cat owners need to understand diabetes management to be able to accomplish these goals.

Highly purified porcine insulin

Caninsulin is an aqueous suspension of 40 IU/mL of highly purified porcine insulin, consisting of 35% amorphous and 65% crystalline zinc insulin.

Porcine insulin has the same amino acid sequence as canine insulin, making it the first choice for dogs^{1,2} and less likely for dogs to develop anti-insulin antibodies.³

Porcine insulin is 3 amino acids different from feline insulin and as such has the closest sequence to feline insulin.⁴

The efficacy and safety of Caninsulin has been proven in clinical trials in dogs^{5,6} and cats^{7,8,9}. Caninsulin also offers you the added security and confidence that come from over 25 years of successful use by veterinarians worldwide.

Choose Caninsulin first to take advantage of proven efficacy, reassuring safety, accurate delivery and global expertise and support

*	7	Live support from experienced veterinary professionals > Partnering with you to help improve pet diabetes care around the world
*	7	Comprehensive and cost effective diabetes care* > Choices to optimize diabetes management and improve compliance
*	<	Closest match to feline insulin Sood choice for cats—alleviates clinical signs by delivering blood glucose targets with remission possible
*	7	Identical to canine insulin 1º choice for dogs – rapid onset and sustained action alleviates clinical signs with low risk of anti-insulin antibodies
*	7	1s veterinary approved insulin for dogs and cats > Security and confidence built on experience and successful use
Recombinant Human Insulin	Caninsulin®	An effective choice for both dogs and cats

^{*} Including choice of presentations and U40 insulin syringe or insulin pen as well as a free app - Pet Diabetes Tracker.

Over 25 years

of helping vets effectively and safely manage diabetes

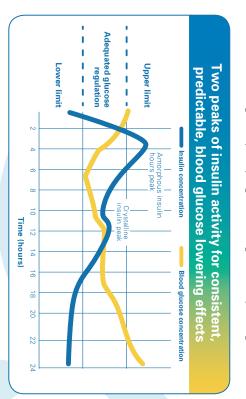
Caninsulin (known as Vetsulin in the USA) is available in more than 45 countries



Benefits of Once or Twice Daily Caninsulin in Dogs

- Rapid onset of effect Amorphous insulin is absorbed rapidly, with activity peaking around 4 hours post-injection⁵
- Sustained effect Crystalline insulin is slowly absorbed, with activity peaking around 11 hours post-injection⁵
- Duration of effect 14 to 24 hours^{6,11,12}, long enough for once daily administration in some cases

At least one-third of dogs adequately regulated using once-daily dosing $^{5.6,10:13}$



Effectively reduces blood glucose and clinical signs of diabetes.⁶



5. Gebran PA et al. J. Small Anim Pract. 1997;28:434-428. 6. Morroe WE et al. J. Vet Insen Med. 2005;19:505-882. 10. Hom B, Mitter RW Aust Vet J. 2000;19:83:1934. 11. Davison I.J. et al. Vet Rec. 2005;19:607-471. 12. Peerson I.M, Bend JS, Morror JM. Vet Rec. 2008;19:4222-237. 13 Fraces Fe t al. Vet Rec. 2018;183:282.



Benefits of Twice Daily Caninsulin in Cats

- Rapid onset and sustained effects Insulin activity generally peaks between 1.5 and 8 hours post-injection^{10,11}
- Duration of effect Effective when administered twice daily^{7-9,15}
- Reassuring safety Helps to minimize the risk of hypoglycemia⁷⁻⁹ compared to twice-daily insulins

Caninsulin provides good to excellent control in the majority of cats^{8,9}

Cats treated with insulin can achieve remission 8.9.74-76

No single factor predicts which cats can achieve remission¹⁴

Controlled diet and weight loss are very important¹⁴⁻¹⁶

Remission independent from type of insulin; no large scale, randomized and controlled studies 16,15

Remission rates of up to 56% have been reported for Caninsulin (without dietary control)8.9.15

Ideal maximum and

blood glucose9*

Effectively reduces blood glucose and reduces clinical signs of diabetes in cats⁷⁻⁹



^{*} Target minimum (nadir) blood glucose 6.3 mmo//L (113 mg/dL) and maximum blood glucose 20.1 mmo//L (360 mg/dL)

^{7.} Aberto E. Esta S. Friendeldom 2019:22-00 8 Abrels tal Hein MuSap 2018 103-90; 8 Marto E. Bard, S. Meite 2019; 1994; 10 Hen E. Materi M. Auffred, 2020 3831-84.
11 Device Lucal Wine 2018; 1994; 11 4 Gestown Read W. L. Out 2022 2022; 11 S. Arickaul Weiterhand, 2010; 24:104-102; 11
13 Supriss M. et al. SPM consense publishes un benotzed monogeneric diabeter melline no at. 2019; 12:22:20.
13 Supriss M. et al. SPM consense publishes un benotzed monogeneric diabeter melline no at. 2019; 12:22:20.



With you for life... Convenient diabetes management

Presentations and Storage*

- \bullet 40 IU/mL concentration for more accurate dosing in dogs and cats requiring low doses (<8 IU per injection)
- Caninsulin offers a variety of presentations:
- 2.5 mL vials
- 10 mL vials
- 2.7 mL cartridges
- Store upright and refrigerated, do not freeze

Dosing*

- Before first use, vials should be shaken thoroughly until a homogeneous, uniformly milky suspension is obtained
- Before each use, invert the vial or cartridge a few times
- Administer with specific U-40 sterile single-use 0.5 or 1.0 mL insulin syringe (vial) or with 0.5 or 1.0 unit increment VetPen® (cartridge)
- Starting with:
- 0.5 to 1 IU insulin/kg body weight per dog, once daily
- 1 to 2 IU per cat per injection, twice daily

Resources

- Consultation services with an experienced pet diabetes professional
- Free Pet Diabetes Tracker app available for pet owner to monitor and share reports with veterinary team
- Multitude of support material available on www.caninsulin.com
- See package insert for full information

FOR LIFE

The first veterinary approved insulin for dogs and cats

You can offer clients a variety of options for BOTH diabetic dogs and cats:





U-40 Insulin Syringe

- Multidose vial offers convenience for pet owners
- Cost-effective delivery option for diabetic pets needing higher doses

VetPen

- The first insulin pen designed exclusively for diabetic pets
- A reassuring option for many owners

NAME OF THE VETERINARY MEDICINAL PRODUCT

Carrinsulin 40 IU/ml Suspension for Injection

QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance

Insulin* 40 IU *(Porcine insulin present as 35% amorphous Zinc insulin and 65%

PHARMACEUTICAL FORM

A white to almost white suspension for injection.

CLINICAL PARTICULARS

Dogs and cats Target Species

Indications for use, specifying the target species

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

Contraindications

must not be administered by the intravenous animals with severe acute diabetes presenting in a ketoacido Caninsulin is a medium duration insulin and is not intended for the tre

Special warnings for each targe

In cats diabetic remission may be poss

Special precautions for use Special precautions for use in anima

Uvariohysterectomy may have to be considered: must be avoided. Care must be taken with the us It is important to establish a strict feeding (oestrus inhibitors) in patients suffering from which will include a minimum of fluctuations

medicinal product to animals Special precautions to be taken by the person adm

package insert or label to the physician be treated by oral administration of glucose. In case of accidental self-injection seek medical advice immediately and show the Accidental self-injection can provoke clinical signs of h

caemia, which should

Adverse reactions (frequency and seriousness)

insulin are extremely rare, although hypersensitivity reactions have been reported. Adverse reactions in dogs and cats associated with administration of porcine

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

progestagens and alpha-2 agonists. Monitoring of glucose levels should be used to adjust dose accordingly. Similarly, changes in diet or exercise routines may alter Changes in insulin requirements may result from administration of substances which alter glucose tolerance such as corticosteroids, thiazide diuretics

Amounts to be administered and administration route

adult responsible for the welfare of the animal. Before Caninsulin is administered, owners should be instructed to have a box of powdered glucose at home. Administration of Caninsulin must be carried out by an

persist after shaking thoroughly can form in insulin suspensions. Do not use the product if visible agglomerates before the product is used and, if required, the product should be gently mixed to maintain a homogeneous, uniformly milky suspension before use. Agglomerates subcutaneous injection. Alternate the injection site daily, Invert the vial or cartridge before use until a homogenous, uniformly milky suspension is obtained. Foam on Caninsulin should be administered once or twice daily, as appropriate, by the surface of the suspension formed during shaking should be allowed to disperse

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 re-usable pen

n two versions. VetPen 8 delivers 0.5 to 8 units unit increments and VetPen 16 delivers 1 to 16 units of increments.

making it necessary to administer an insulin dose In diabetic cats, it is necessary to administer

deficit in the animal's own insulin production

action, twice daily administration of insulin may be necessary. In a clinical study conducted using Camissulin, the majority of diabetic dogs treated required twice daily administration in order to achieve adequate control. In such cases, the dose per injection must be decreased by 25% so that the total daily dose is less than doubled. made more frequently than every 3 to 7 days. Depending on the duration of insulin serial blood glucose measurement. Alterations in dose should not normally be ding to the evolution of the diabetes clinical signs and to the results uent adjustment to establish the maintenance starting dose of 0.5 to 1 IU/kg bodyweight ntire number of units. To reduce the risk o

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. Fur ther dose adjustments should be made progressively as previously explained.

To achieve a balance between the generation of glucose and the effect of the time of peak insulin effect should be constant. In dogs treated once daily, the second meal is usually fed at 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

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

starting dose should not exceed 2 IU per injection. Cat: The initial dose is 0.25 IU/kg or 0.5 IU/kg per injection as presented below. The

Cats require twice daily administration.

maximum of 2 IU per injection) <20 mmol/1 or <3.6 g/1 (<360 mg/dl) Cat blood glucose concentration Starting dose per cat 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

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

frequent increases in dose are not recommended. and the variations in insulin responsiveness that are seen with time, larger or 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, increasing or decreasing the daily dose according to the results of serial blood glucose measurement. Alterations in dose should not normally be made more Subsequent adjustment to establish the maintenance dose should be made by

Maintenance phase in dogs and cats

requirement. This includes clinical monitoring to deto manage the animal in such a way as to minimise the varia Once the maintenance dose has been reached and the animal is stabilised, insulin and adjustment of dose if required. long-term management programme needs to be established.

Follow up examinations should be perforn (dogs), fatty liver (dogs and cats), etc.

concentration). Monitoring of urine glucose (if with and following the recommendations of the Adjustments to the insulin dose should be made clinical signs supported by the laboratory results, emergency procedures, antidotes), if necessary glucose and biochemical parameters (like bl if there are problems) to monitor the animal

the rear legs and disorientation indicate progression of immediate administration of glucose solution and food to Overdose of insulin results in clinical signs of hypogly increasing anxiety, unstable locomotion, muscle twite ne blood glucose and requires

overdose of insulin insufficient to cause, potentially fatal, hypoglycaemia. As hypoglycaemia begins to develop, a hormoral response is triggered which results in the rebease of glucose from hepaice gloogen stores. This results in rebound hyperglycaemia which may also manifiest as glycosuria for part of the day. There is a danger that the Somogyi overswing is interpreted as a requirement for increase in the insulin dose rather than a decrease. This situation can progress to an overdose so large as to cause clinical hypoglycaemic effects. This can be avoided Somogyi overswing, also called rebound hyperglycaemia, is a response to an hyperglycaemia and respond appropriately is very important. point measurements. The ability of pet owners to recognize the signs of hypo-or by basing decisions on serial blood glucose measurements rather than single

Pharmacodynamic properties

porcine insulin is a naturally occurring hormone produced by the pancreas by the beta cells in the Islets of Langerhans. The overall effect of insulin is to promote an anabolic state in which there is a net synthesis of carbohydrate, protein and fat Caninsulin is an intermediate acting insulin product containing porcine insulin, which is structurally identical to canine insulin. The active ingredient highly purified

Insulin facilitates the intake of glucose obtained from food or gluconeogenesis and brain in particular utilise large amounts of glucose. In diabetes mellitus there is a decreased use of glucose caused by a relative or absolute insulin deficiency. Entrance of glucose into cells is therefore inhibited and glucose accumulates in the body fluids. by cells that are in need of energy supply for metabolism. Liver, adipose tissue

Pharmacokinetic particulars

injection. diabetic dogs, the action of Canisulin in blood plucose concentrations, following subcutaneous administration peaks at about 4-81 post-injection and less for 14-24. In Indiabetic cast the action of Canisulino no blood glucose concentrations after subcutaneous administration peaks at about 4-6 hours and lest for 8-12 hours post which exerts an effect at about 3h after subcutaneous injection and has a duration of effect of about 6-8h, and 65% crystalline insulin which has a slower onset and a maximum effect between 7-12h after injection and a duration of 16-24 hours. In The product is an intermediate acting product containing 35% amorphous insulin,

udies, this veterinary medicinal product must not

Shelf life after first opening: 28 days.

and refrigerated at between +2 and

The pen containing a cartridge should not be stored in the refrigerator. The pen cap must be put back on the pen after each injection in order to protect from light. Keep the vial or unopened cartridge in the outer carton. opening, store below 25°C and away from direct heat or direct light.

Any unused product or waste material should be disposed of in accordance with products or waste materials derived from the use of such products Special precautions for the disposal of unused veterinary medicinal

national requirements.

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



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^{1,2} suitable for once or twice daily administration
- A good choice for cats with comparable remission rates to other commonly used twice-daily insulins^{14,15}
- 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 for your clinic
- www.pet-diabetes.com for pet owners
- Training Videos and Materials
- 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

Behrend E et al. J Am Anim Hosp Assoc. 2018; 54:1–21. 2. Ackerman N et al. Companion Animal. 2018;23:143-151.
 Gostelow R et al. Vet J. 2014;202:208-221. 15. Zini E et al. J Vet Intern Med. 2010;24:1314-1321.

