

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

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

* Including choice of presentations and U40 insulin syringe or VetPen[®] insulin delivery pen as well as a free app - **Pet Diabetes Tracker**.

Over 25 years

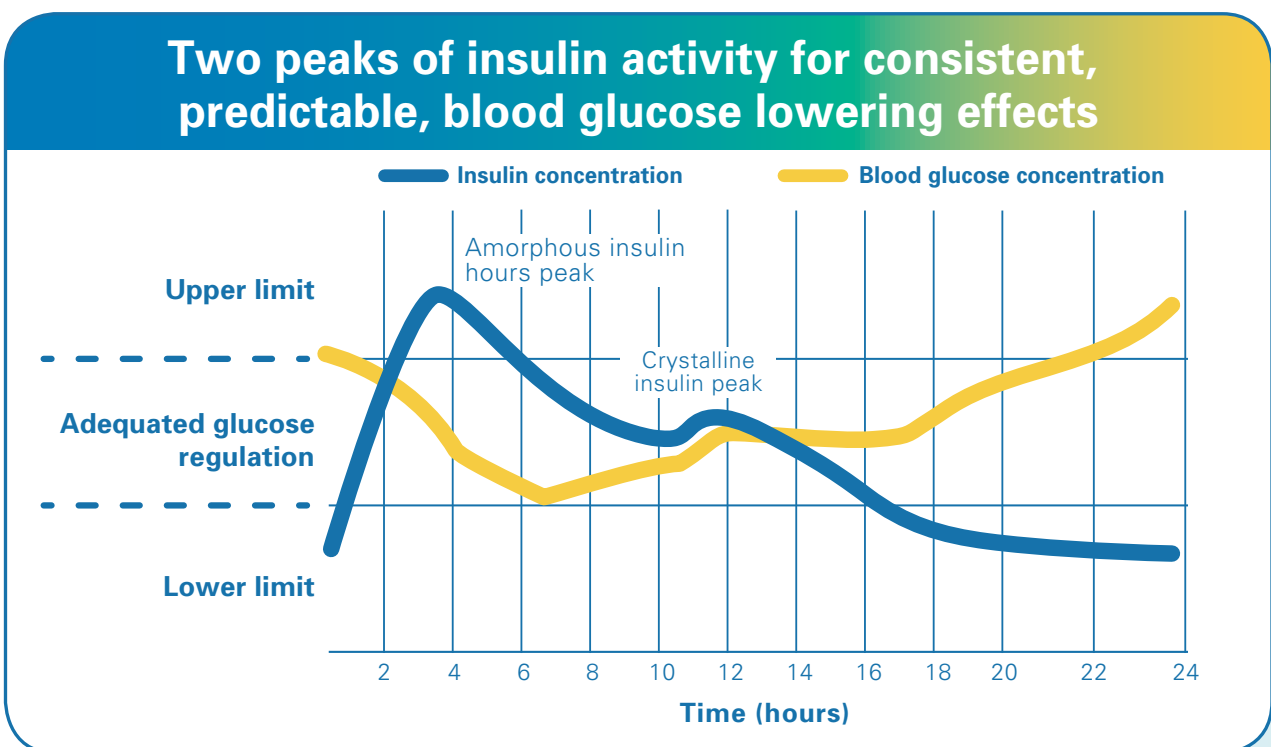
of helping veterinarians effectively and safely manage diabetes

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

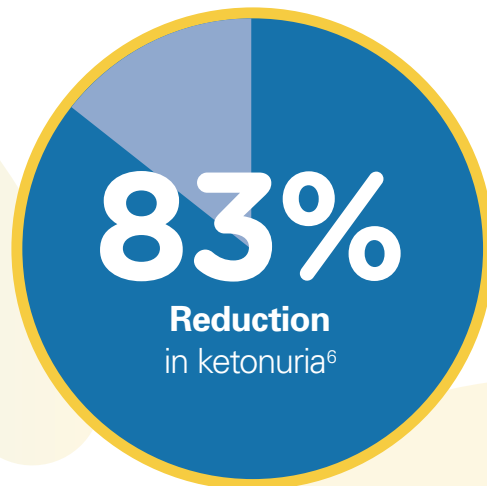
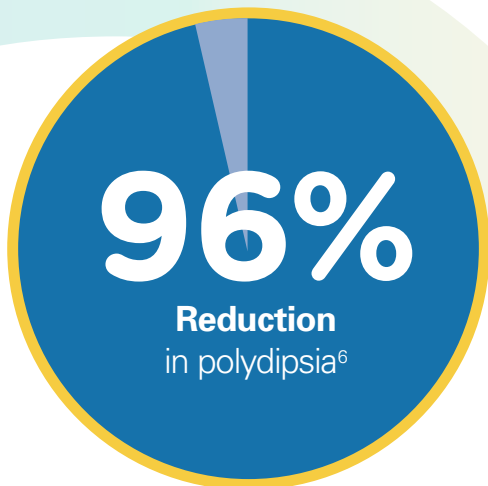
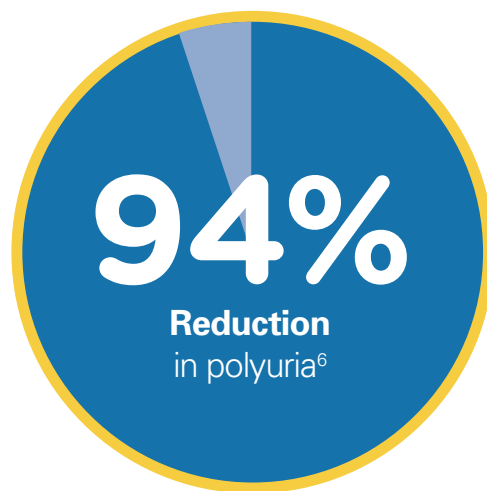
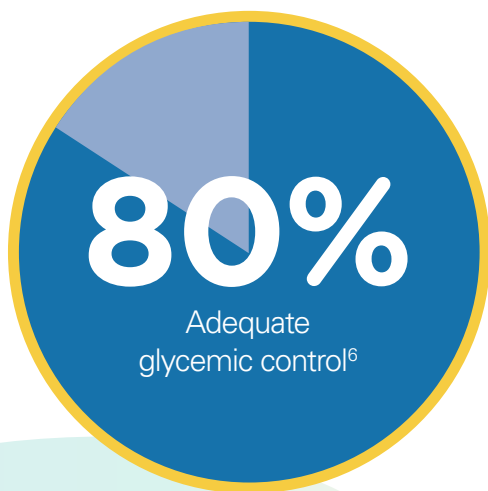
Benefits of Once or Twice Daily Caninsulin® in Dogs

- **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





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}

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

Cats treated with insulin can achieve remission^{8,9,14-16}

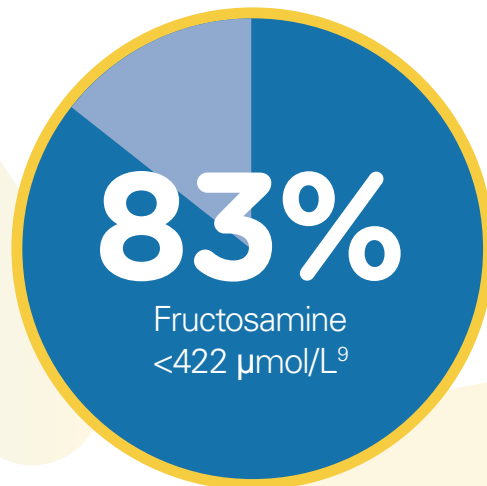
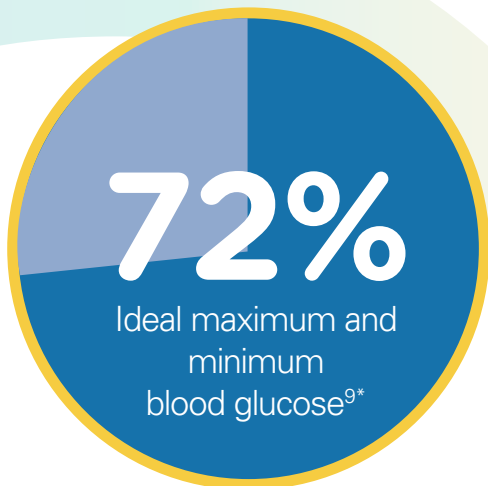
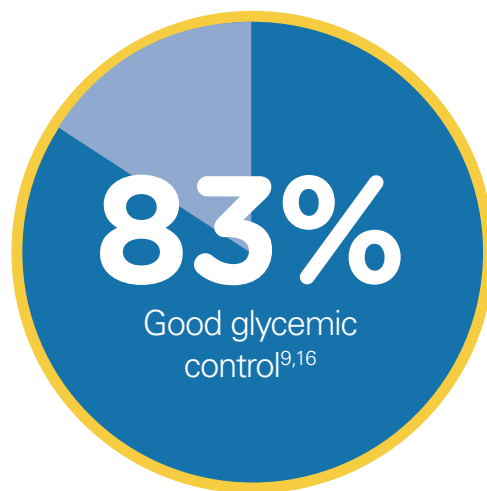
No single factor predicts which cats can achieve remission¹⁴

Controlled diet and weight loss are very important¹⁴⁻¹⁶

Remission independent from type of insulin; no large scale, randomized and controlled studies^{14,15}

Remission rates of up to 56% have been reported for Caninsulin (without dietary control)^{8,9,15}

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



* Target minimum (nadir) blood glucose 6.3 mmol/L (113 mg/dL) and maximum blood glucose 20.1 mmol/L (360 mg/dL)

With you for life...

Convenient diabetes management

Presentations and Storage*

- 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 in the dark, 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 I.U. per kg of body weight per dog, once daily
 - 0.25 - 0.5 I.U. per kg of body weight per cat, twice daily

Resources

- Consultation services with an experienced Technical Services Veterinarian
- 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.ca

* See package insert for full information.



WITH YOU 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
- The only insulin injection pen approved for veterinary use in Canada
- A reassuring option for many owners

Caninsulin®

Merck Animal Health

PORCINE INSULIN ZINC INJECTION (Mfr. Std.)

STERILE SUSPENSION, 40 I.U./ML

DIN 02052474, DIN 02416239

FOR VETERINARY USE ONLY

DESCRIPTION: Caninsulin is an intermediate-acting insulin. Each mL contains highly purified porcine insulin 40 IU (Ph. Eur.) consisting of 35% amorphous zinc insulin and 65% crystalline zinc insulin ("Lente" type). Non medicinal ingredients: (per mL): zinc chloride 0.08 mg, sodium acetate trihydrate 1.36 mg, sodium chloride 7.0 mg and methyl parahydroxybenzoate 0.1% (as preservative).

INDICATIONS: For the control of hyperglycemia associated with diabetes mellitus in dogs and cats.

DOSE AND ADMINISTRATION: The starting dose is calculated based on the dog's or cat's body weight as directed in the Table below. Dose-titration is necessary to meet the treatment needs of each individual animal. After a period of acclimatization, a blood glucose curve should be determined and the dose adjusted to achieve satisfactory long term control (see Monitoring and Dose Adjustment section below).

RECOMMENDED STARTING DOSES: Dogs: 0.5 I.U. per kg of body weight once daily, rounded down to the lowest entire number of units. Some examples are given in the table below.

Cats: 0.25 - 0.5 I.U. per kg of body weight, for a maximum of 2 I.U. per dose, based on blood glucose concentration at diagnosis, as presented in the Table below. Cats require twice daily administration.

Dogs	
Body Weight	Starting Dose
5 kg	2 I.U. once daily
10 kg	5 I.U. once daily
15 kg	7 I.U. once daily
20 kg	10 I.U. once daily

Cats	
Blood Glucose Concentration	Starting Dose
< 20 mmol/L or < 3.6 g/L (360 mg/dL)	0.25 I.U./kg twice daily
≥ 20 mmol/L or ≥ 3.6 g/L (360 mg/dL)	0.5 I.U./kg twice daily

Subsequent adjustment to establish the maintenance dose should be made by increasing or decreasing the dose according to clinical signs and serial blood glucose measurements (see Monitoring and Dose Adjustment below).

ADMINISTRATION: With vials, the use of U-40 insulin syringes is strongly recommended to ensure accurate dosing. The cartridge is designed to be used **only** with VetPen® and 29 G/12 mm single use needles. VetPen® is accompanied by a package leaflet with detailed instructions for use to be followed.

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. In case the suspended particles have settled during the waiting period, the product should be mixed again, gently this time, prior to use, to maintain a homogeneous, uniformly milky suspension.

Turn **the cartridge** up and down at least 10 times until the insulin appears uniformly milky.

Do not use if clumps, particles, or flocculation are visible after mixing.

The contents should be used within 6 weeks (vials) or 28 days (cartridges) and stored below 25°C after the first dose is removed.

Inject subcutaneously 2 to 5 cm from the dorsal midline on alternating sides, varying from behind the scapula to the mid-lumbar region. Veterinarians should instruct pet owners on proper storage and handling, show them how to draw the insulin from the bottle, and instruct them on how to administer Caninsulin.

DIET: A nutritionally complete commercial dry or canned pet food should be fed in consistent amounts and at consistent times each day, according to the veterinarian's recommendations. Animals receiving Caninsulin injections once daily should be fed 1/2 to 2/3 of their caloric requirement at the time of injection and 1/2 to 1/3 of their requirement approximately 8 to 10 hours later, depending on the client's schedule. Animals receiving Caninsulin injections twice daily should be fed 1/2 of their caloric requirement at the time of each injection.

MONITORING AND DOSE ADJUSTMENT: Since the times to the peaks and the duration of insulin activity from Caninsulin will vary among animals, the dose should be adjusted based on the measurement of blood glucose levels. They should be determined 2 to 4 hours after each injection for the first 2 days to assure the animal is not becoming dangerously hypoglycemic (blood glucose < 80 mg/dL, 4.4 mmol/L). The animal should then be allowed to acclimate to this treatment 4 to 5 days before determining the glucose curve and adjusting the dose. A glucose curve should be obtained by administering Caninsulin, feeding the animal as described under the DIET section, and measuring blood glucose every 1 to 2 hours for 24 hours. In dogs and cats, the dose should then be adjusted by 10 percent per day until the lowest blood glucose is approaching normal glycemia or between 4.4 - 6.6 mmol/L (80-120 mg/dL). While adjusting the dose, the blood glucose should be measured 2 or 3 times daily, at the times when it is expected to be lowest as determined by the glucose curve, and just before the next dose is to be given.

Once the dose that will reduce blood glucose to 4.4 - 6.6 mmol/L (80-120 mg/dL), is established, the blood glucose curve may need to be repeated to accurately determine the peaks and duration of activity resulting from this dose. In dogs administered Caninsulin once daily, if the duration of insulin action is less than 16 hours (blood glucose is reduced to 4.4 - 6.6 mmol/L (80-120 mg/dL), but increases to 13.9 mmol/L (250 mg/dL) less than 16 hours after administration), Caninsulin may be given twice daily at 12 hour intervals. Initially, the 2 doses should be equal and each dose should be 25% less than the dose that reduced the blood glucose to between 4.4 - 6.6 mmol/L (80-120 mg/dL), when Caninsulin was given once daily. The doses should then be adjusted as described above. The dose given in the evening may be less than the dose given in the morning, if control of hyperglycemia is improved by doing so.

As an alternative, the insulin dose can be adjusted, based on daily measurement of morning urine glucose levels by the client. Although this is an acceptable method, it is not recommended as the sole criterion upon which to adjust the dose, because factors other than insulin dose can affect urine glucose concentration. In dogs and cats, the aim should be to manage the diabetic animals so as to reduce or eliminate the clinical signs of diabetes mellitus whilst minimizing the occurrence of hypoglycemia; obtain normal blood glucose concentrations between 5-14 mmol/l (100-250 mg/dL) in the dog and 5-17 mmol/l (100-300 mg/dL) in the cat; attain and/or maintain normal bodyweight, and to minimize and/or eliminate polydipsia, polyuria, and polyphagia (if present). In the cat, since clinical diabetic remission may be possible, it is important to monitor for signs of hypoglycemia.

Once adequate control is achieved, the animal should be re-examined in one week. If control remains adequate at that time, regular examinations should be scheduled at 3 to 4 month intervals, or whenever the client notes one or more of the following: Polydipsia (daily water consumption > 70 ml per kg of body weight for 3 or more days); Polyuria; Inappetance or anorexia, polyphagia; Loss of body weight or condition; Weakness and/or dizziness.

If control is found to be inadequate, the dose or doses should be re-adjusted as described above. The blood glucose curve may also need to be repeated.

OVERDOSE: If the dog or cat shows signs of hypoglycemia: weakness, confusion, dizziness or seizures, the animal should be re-examined immediately. In mild cases offer the animal its usual food. More serious symptoms can be treated with an oral dextrose solution or corn syrup rubbed on the oral mucosa or an intravenous injection of a 50% dextrose solution.

CONTRAINDICATIONS: Do not inject intravenously. Caninsulin is not to be administered to hypoglycemic or anorexic dogs or cats. Dogs and cats known to have a systemic allergy to pork or pork products should not be treated with Caninsulin.

CAUTIONS: Animals which present with severe ketoacidosis, anorexia and/or vomiting should be stabilized with short acting insulin before beginning treatment with Caninsulin. Stress and irregular extra exercise must be avoided. Diabetic control is best achieved in spayed bitches and queens. Therefore, intact diabetic females should be spayed as soon as they are stable enough to withstand the procedure. The use of progestogens (estrus inhibitors) and long acting glucocorticoids in patients suffering from diabetes mellitus should be avoided. The concurrent administration of drugs known to lower blood glucose such as oral hypoglycemic drugs is not recommended. Depending on the etiology of the diabetes mellitus insulin therapy alone may not be sufficient and additional diagnostics and treatment may be required.

WARNINGS: Avoid contact with eyes. In case of contact, immediately flush eyes with copious amounts of water for 15 minutes. Accidental injection may cause clinical hypoglycemia. In case of accidental injection, seek medical attention immediately. Exposure to product may induce a local or systemic allergic reaction in sensitized individuals. **KEEP OUT OF THE REACH OF CHILDREN.**

ADVERSE REACTIONS: Local injection site reactions have been reported rarely in dogs and very rarely in cats. These reactions are usually mild and reversible. In very rare cases, allergic reactions to porcine insulin have been reported.

Although all adverse reactions are not reported, the following adverse reaction information is based on voluntary post-approval drug experience reporting. It is generally recognized that this method of reporting results in significant under-reporting of adverse drug reactions.

It should be noted that suspected adverse reactions listed here reflect reporting and not causality. The following adverse reactions are listed in decreasing order of frequency.

Adverse events in **cats** include: lack of effectiveness/dysregulation, decreased appetite/anorexia, vomiting, lethargy, death, injection site reaction, hypoglycemia, ataxia, diarrhea, seizures, and polyuria/polydipsia.

Adverse events in **dogs** include: lack of effectiveness/dysregulation, lethargy, allergic or skin reaction, vomiting, hypoglycemia, injection site reaction, ataxia, decreased appetite/anorexia, seizures, and diarrhea.

PHARMACOLOGY: Canine and feline diabetes mellitus is an endocrinopathy resulting from relative or absolute insulin deficiency. Insulin deficiency impairs cellular uptake of glucose and promotes hepatic gluconeogenesis. When the renal threshold for glucose is exceeded, glucosuria results, along with osmotic diuresis leading to polyuria and polydipsia. Unmanaged diabetes results in ketosis, ketoacidosis, and if left untreated, acidosis, coma and death. Most forms of canine or feline diabetes can be successfully managed by controlling hyperglycemia with regular administration of exogenous insulin and dietary manipulation. The amino acid structure of porcine insulin is identical to the amino acid structure of canine insulin and 3 amino acids different from feline insulin.

In dogs, the amorphous fraction of Caninsulin gives a peak of activity at approximately 3 hours and a duration of action of approximately 8 hours. The crystalline fraction gives a peak of activity at 7 to 12 hours and a duration of activity of approximately 24 hours. In cats, Caninsulin has a peak of activity at approximately 4-6 hours post-administration and a duration of activity of 8 to 12 hours. Accordingly, Caninsulin should be administered once daily in dogs and twice daily in cats. However, the times to the peaks and durations of insulin activity from Caninsulin will vary among individual animals.

STORAGE: Refrigerate at 2-8°C. Store in an upright position, in the dark. Do not freeze.

HOW SUPPLIED: Box of 10 x 2.5 mL vials; Box of 1 x 10 mL vial; Box of 10 x 2.7 mL cartridges (for use only with VetPen® insulin delivery pen)

For further information please refer to the Client Information Sheet which can be found at www.caninsulin.ca

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CPN: 1208132.6

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.ca
- 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.ca or ask your Merck Animal Health Representative today

1. Behrend E et al. J Am Anim Hosp Assoc. 2018; 54:1–21. 2. Ackerman N et al. Companion Animal. 2018;23:143-151. 14. Gostelow R et al. Vet J. 2014;202:208-221. 15. Zini E et al. J Vet Intern Med. 2010;24:1314-1321.