



TRANSITIONING CANINE PATIENTS WITH DIABETES MELLITUS TO VETSULIN® (PORCINE INSULIN ZINC SUSPENSION)*

1. IS THE DOG ADEQUATELY REGULATED ON ITS CURRENT (HUMAN) INSULIN?

YES

NO

2. VETERINARIAN/OWNER WANTS TO TRY VETSULIN S.I.D.

2. VETERINARIAN/OWNER WANTS TO TRY VETSULIN B.I.D.

2. INVESTIGATE THE REASON FOR INADEQUATE REGULATION. IS POOR GLYCEMIC CONTROL:

- | | | |
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| <p>Associated with a human factor?</p> <ul style="list-style-type: none"> • Is someone new giving the insulin? • Is the correct syringe being used? • Is the insulin mixed gently and properly? • Is the correct dose being drawn into the syringe? • Is the insulin injected correctly (i.e., subcutaneously, not intradermally)? • Is the injection site being located correctly? • Are treats being fed? • Does the dog eat other pets' food? | <p>Caused by insulin therapy?</p> <ul style="list-style-type: none"> • Is the insulin being stored correctly: <ul style="list-style-type: none"> → Refrigerated at the correct temperature? → Stored upright? → Refrigerated, not frozen? → Refrigerated between doses? • What is the expiration date of the insulin? • Is the insulin being diluted? • Has the insulin been used for longer than a month? | <p>Caused by concurrent disorder?</p> <ul style="list-style-type: none"> • Canine Cushing's syndrome (hyperadrenocorticism) • Infection (i.e., dental, skin, urinary tract) • Hypothyroidism • Obesity • Pancreatitis • Exocrine pancreatic insufficiency • Diestrus • Concurrent medications (e.g., steroids) |
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Yes to any confounding factor: Resolve the identified issues and rule out possible concurrent disorders that may be contributing to inadequate regulation before initiating Vetsulin treatment.

No to all factors: Begin Vetsulin therapy to reduce hyperglycemia and related clinical signs in diabetic dogs.

3. SWITCHING A PATIENT FROM HUMAN LENTE OR NPH INSULIN [HUMULIN® (HUMAN INSULIN [rDNA ORIGIN] ZINC SUSPENSION)] TO VETSULIN S.I.D.

- Discontinue evening dose of human insulin
- The next morning, administer the same number of units of Vetsulin as would have been given of human insulin (e.g., a dog receiving 20 IU human insulin b.i.d. would be given 20 IU Vetsulin s.i.d.). However, twice-daily dosing may be necessary for optimal control.

3. SWITCHING A PATIENT FROM HUMAN LENTE OR NPH INSULIN TO VETSULIN B.I.D.

- Discontinue human insulin
- Use an initial dose of Vetsulin that is 75% of the previous human insulin dose (e.g., a dog receiving 20 IU human insulin b.i.d. would be given 15 IU Vetsulin b.i.d.).

3. SWITCHING AN INADEQUATELY REGULATED PATIENT FROM HUMAN INSULIN TO VETSULIN THERAPY

- Discontinue current (human) insulin
- Weigh dog
If the dog's body weight in kilograms (kg) is a fraction, round down the body weight (e.g., a 12.9-kg dog would be dosed as a 12-kg dog). If the dog is grossly overweight, use the optimal body weight to calculate the initial Vetsulin dosage.
- Establish the starting dosage based on the labeled dose (see chart).

Body Weight	Dose + Dose Supplement	Initial Dose
<10 kg (<22 lbs)	(Weight in kg) x 1 IU/kg + 1 IU	1 IU/kg + 1 IU
10–11 kg (22–24 lbs)	(Weight in kg) x 1 IU/kg + 2 IU	1 IU/kg + 2 IU
12–20 kg (25–44 lbs)	(Weight in kg) x 1 IU/kg + 3 IU	1 IU/kg + 3 IU
>20 kg (>44 lbs)	(Weight in kg) x 1 IU/kg + 4 IU	1 IU/kg + 4 IU

- Begin Vetsulin therapy with s.i.d. administration.

4. EVALUATE PATIENT 5–7 DAYS AFTER STARTING VETSULIN

ASK OWNER ABOUT CHANGES IN CLINICAL SIGNS

- Has the dog's water drinking increased, decreased or stayed the same since your last visit?
- Has the frequency of your dog's urination changed since your last visit? Has the volume of urine changed?
- How is your dog's activity level? Does his/her activity seem normal? Or does he/she seem sluggish or too active?
- When you go for walks, does your dog tire easily?

WEIGH DOG

- Has there been any significant change in weight?

GENERATE SERIAL BLOOD GLUCOSE CURVE

5. WHAT IS THE LOWEST BLOOD GLUCOSE LEVEL?

<100 mg/dl (<5.6 mmol/L)

Decrease insulin dose by 10% and reevaluate in 5–7 days

100–150 mg/dl (5.6–8.3 mmol/L)

>150 mg/dl (>8.3 mmol/L)

Increase insulin dose by 10% and reevaluate in 5–7 days

6. IF S.I.D. DOSING, WHAT IS THE DURATION OF INSULIN EFFECT?

Blood glucose begins to increase above 200–250 mg/dl <14–18 hours after s.i.d. dose

Initiate b.i.d. Vetsulin dosing
• Reduce Vetsulin dose by 25% and administer twice daily

Reevaluate patient in 5–7 days

Blood glucose begins to increase above 200–250 mg/dl >14–18 hours after s.i.d. dose

Continue to administer Vetsulin s.i.d.

Reevaluate patient in 2–4 months



FEEDING PLAN:

Once-Daily Insulin Administration

- Feed the first meal (e.g., 2/3 of the daily ration) prior to the morning insulin injection.
- Feed the second meal (the remainder of the daily ration) about 8–10 hours later.

Twice-Daily Insulin Administration

- Feed the first small meal (1/2 of the daily ration) prior to the morning insulin injection.
- Feed the second meal (the remainder of the daily ration) 12 hours later and prior to the afternoon/evening insulin injection.

GENERAL RECOMMENDATIONS:

1. The dose will most likely need to be adjusted until adequate regulation is achieved.
2. Dose adjustments should be based on clinical signs and evaluation of a serial glucose curve.
3. Allow 5–7 days between dose changes.
4. Dose adjustments should be in increments of 10% of the current dose.
5. Educate the client on the need for and importance of using U-40 syringes with Vetsulin.

*Vetsulin is known as Caninsulin® in Canada, Europe and Australia.

PRODUCT INFORMATION

NADA NO. 141-236, Approved by FDA
Vetsulin® (PORCINE INSULIN ZINC SUSPENSION)

CAUTION

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION

Vetsulin® is a sterile aqueous zinc suspension of purified porcine insulin.

Each mL contains:

Purified porcine insulin (30% amorphous and 70% crystalline)	40 IU
Zinc chloride	0.08 mg
Sodium acetate trihydrate	1.36 mg
Sodium chloride	7.0 mg
Methylparaben (preservative)	1.0 mg

pH is adjusted with hydrochloric acid and/or sodium hydroxide.

INDICATION

Vetsulin® (porcine insulin zinc suspension) is indicated for the reduction of hyperglycemia and hyperglycemia-associated clinical signs in dogs with diabetes mellitus.

DOSAGE AND ADMINISTRATION

USE OF A SYRINGE OTHER THAN A U-40 SYRINGE WILL RESULT IN INCORRECT DOSING.
FOR SUBCUTANEOUS INJECTION IN DOGS ONLY

Vetsulin® should be mixed by gentle rolling of the vial prior to withdrawing the dose from the vial. Using a U-40 insulin syringe, the injection should be administered subcutaneously, 2 to 5 cm (3/4 to 2 in) from the dorsal midline, varying from behind the scapulae to the mid-lumbar region and alternating sides.

The initial recommended Vetsulin® dose is 1 IU insulin/kg body weight plus a body weight-dependent dose supplement as shown in the table below.

Body Weight	Dose	+	Dose Supplement	Initial Dose
<10 kg (<22 lb)	(Weight in kg) x 1 IU/kg		1 IU	1 IU/kg + 1 IU
10 - 11 kg (22 - 24 lb)	(Weight in kg) x 1 IU/kg		2 IU	1 IU/kg + 2 IU
12 - 20 kg (25 - 44 lb)	(Weight in kg) x 1 IU/kg		3 IU	1 IU/kg + 3 IU
>20 kg (>44 lb)	(Weight in kg) x 1 IU/kg		4 IU	1 IU/kg + 4 IU

Initially, this dose should be given once daily concurrently with, or right after a meal. The veterinarian should re-evaluate the dog at appropriate intervals and adjust the dose based on clinical signs, urinalysis results, and glucose curve/spot check values until adequate glycemic control has been attained. In the US clinical study, glycemic control was considered adequate if an acceptable blood glucose curve was achieved (reduction in hyperglycemia and a nadir of 60-160 mg/dL), clinical signs of hyperglycemia (polyuria, polydipsia, and ketonuria) were improved, and hypoglycemia (blood glucose <50 mg/dL) was avoided. Twice-daily therapy should be initiated if the duration of insulin action is determined to be inadequate. If twice-daily treatment is initiated, the two doses should be 25% less than the once daily dose required to attain an acceptable nadir.

Further adjustments in dosage may be necessary with changes in the dog's diet, body weight, or concomitant medication, or if the dog develops concurrent infection, inflammation, neoplasia, or an additional endocrine or other medical disorder.

CONTRAINDICATIONS

Dogs known to have a systemic allergy to pork or pork products should not be treated with Vetsulin®. Vetsulin® is contraindicated during periods of hypoglycemia.

WARNINGS

User Safety: For use in animals only. Keep out of the reach of children. 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.

Animal Safety: Use of this product, even at established doses, has been associated with hypoglycemia. An animal with signs of hypoglycemia should be treated immediately. Glucose should be given orally or intravenously as dictated by clinical signs. Insulin should be temporarily withheld and, subsequently, the dosage should be adjusted, if indicated.

Any change in insulin should be made cautiously and only under a veterinarian's supervision. Changes in insulin strength, manufacturer, type, species (animal, human) or method of manufacture (rDNA versus animal-source insulin) may result in the need for a change in dosage.

Appropriate diagnostic tests should be performed to rule out endocrinopathies, especially hyperadrenocorticism in diabetic dogs that are difficult to regulate.

PRECAUTIONS

Animals presenting with severe ketoacidosis, anorexia, lethargy, and/or vomiting should be stabilized with short-acting insulin and appropriate supportive therapy until their condition is stabilized. As with all insulin products, careful patient monitoring for hypoglycemia and hyperglycemia are essential to attain and maintain adequate glycemic control and associated complications. Overdosage can result in profound hypoglycemia and death. Progestogens, certain endocrinopathies and glucocorticoids can have an antagonistic effect on insulin activity. Intact bitches should be ovariectomized. Progestogen and glucocorticoid use should be avoided.

Drug Interactions: In the US clinical effectiveness study, dogs received various medications while being treated with Vetsulin® including antimicrobials, NSAIDs, thyroid hormone supplementation, internal and external parasiticides, anti-emetics, dermatological topical treatments and oral supplements, and ophthalmic preparations containing antimicrobials and antiinflammatories. No medication interactions were reported. This drug was not studied in dogs receiving steroids.

Reproductive Safety: The safety and effectiveness of Vetsulin® in breeding, pregnant, and lactating dogs has not been evaluated.

Use in puppies: The safety and effectiveness of Vetsulin® in puppies has not been evaluated.

ADVERSE REACTIONS

In the field effectiveness and safety study, 66 dogs were treated with Vetsulin®. Sixty-two dogs were included in the assessment of safety. Hypoglycemia with or without associated clinical signs occurred in 35.5% (22/62) of the dogs at various times during the study. Clinical signs of hypoglycemia were generally mild in nature (described as weakness, lethargy, stumbling, falling down, and/or depression). Disorientation and collapse were reported less frequently and occurred in 16.1% (10/62) of the dogs. Two dogs had a seizure and one dog died during the seizure. Although never confirmed, the presumptive diagnosis was hypoglycemia-induced seizures. In the rest of the dogs, hypoglycemia resolved with appropriate therapy and adjustments in insulin dosage.

Seven owners recorded the following observations about the injection site on the home monitoring forms: swollen, painful, sore, and a bleb under the skin.

The following clinical observations occurred in the field study following treatment with Vetsulin® and may be directly attributed to the drug or may be secondary to the diabetic state or other underlying conditions in the dogs: hematuria, vomiting, diarrhea, pancreatitis, non-specific hepatopathy/pancreatitis, development of cataracts, and urinary tract infections.

During the 1995-2001 period, the following adverse reactions in 19 dogs treated with porcine insulin zinc suspension were reported to Intervet International: destabilization (defined as lack of adequate regulation), lack of expected efficacy, edema of the head and neck, development of a fibrous lump at the injection site, hypoglycemia and death following administration of typical doses (one death in two dogs) and overdosage (four deaths in four dogs).

To report adverse reactions, call 1-800-345-4735.

INFORMATION FOR DOG OWNERS

Please refer to the Client Information sheet for more information about Vetsulin®. Vetsulin®, like other drugs of this class, is not free from adverse reactions. Owners should be advised of the potential for adverse effects and be informed of the associated clinical signs. Potential adverse reactions include hypoglycemia, insulin antagonism/resistance, rapid insulin metabolism, insulin-induced hyperglycemia ("Somogyi Effect"), and local or systemic reactions. The primary adverse reaction observed is hypoglycemia. Signs may include weakness, depression, behavioral changes, muscle twitching, and anxiety. In cases of severe hypoglycemia seizures and coma can occur. Hypoglycemia can be fatal if an affected dog does not receive prompt treatment. Appropriate veterinary monitoring of blood glucose, adjustment of insulin dose and regimen as needed, and stabilization of diet and activity help minimize the risk of hypoglycemic episodes. The attending veterinarian should evaluate other adverse reactions on a case-by-case basis to determine if an adjustment in Vetsulin® therapy is appropriate, or if alternative therapy should be considered.

GENERAL PHARMACOLOGY

Porcine insulin is similar in amino acid structure to canine insulin. Vetsulin® is classified as an intermediate acting insulin. Vetsulin® has two peaks of activity following subcutaneous administration (the first at around 4 hours and the second at around 11 hours) (1). The duration of activity varies between 14 and 24 hours (1). The peak(s), duration of activity and dose required to adequately control diabetic signs will vary between dogs.

EFFECTIVENESS

A total of 66 client-owned dogs were enrolled in and 53 completed the effectiveness and safety field study. The patients completing the study included 22 breeds of purebred and various mixed breed dogs ranging in age from 4.8 to 14 years, and ranging in weight from 4.2 to 51.3 kg. Of the dogs completing the study, 25 were spayed females and 28 were male (21 neutered and 7 intact).

Dogs were started on Vetsulin® at a dose of 1 IU/kg plus a body weight-dependent dose supplement once daily. The initial treatment time to reach acceptable glycemic control (Dose determination period) ranged from 5 to 151 days. Dogs were evaluated for treatment effectiveness three times at 30-day intervals (Study Period). The blood glucose curve means and mean nadirs were compared pre- and post-treatment to assess effectiveness. The blood glucose curve mean was reduced from 370 mg/dL pre-treatment to 151 mg/dL, 185 mg/dL, and 184 mg/dL at the three treatment period evaluations. The blood glucose mean nadir was reduced from 315 mg/dL pre-treatment to 93 mg/dL, 120 mg/dL, and 119 mg/dL at the three treatment period evaluations. Sixty days after an adequate Vetsulin® dose was initially established, 94%, 96% and 83% of study dogs experienced a reduction in polyuria, polydipsia, and ketonuria, respectively. Investigators reported adequate glycemic control an average of 81% of the time during the Study Period.

The injection frequency and effective dose range for dogs varied substantially:

Study Time	Dogs on SID therapy	Dogs on BID therapy	Range of SID doses (IU/kg)	Range of BID doses (IU/kg)	
				a.m. dose	p.m. dose
Time 0 (Initial dose)	51 (96%)	2 (4%)	0.94 - 1.28	1.06 - 1.07	1.06 - 1.07
Time 1	23 (43%)	30 (57%)	0.44 - 2.22	0.39 - 1.29	0.39 - 1.26
Time 2	23 (43%)	30 (57%)	0.33 - 2.19	0.40 - 1.25	0.39 - 1.22
Time 3	18 (34%)	35 (66%)	0.43 - 2.18	0.34 - 1.40	0.28 - 1.40

HOW SUPPLIED

Vetsulin® is supplied as a sterile injectable suspension in multidose vials containing either 2.5 mL or 10 mL of 40 IU/mL porcine insulin zinc suspension. Vials are supplied in cartons of one, 10 mL vial and cartons of ten, 2.5 mL vials.

STORAGE CONDITIONS

Store in an upright position under refrigeration at 2° to 8° C (36° to 46° F). Do not freeze. Protect from light.

Distributed by: INTERVET INC.

Millsboro, DE 19966

Made in Holland

References

1. Graham P, Nash A, McKellar Q. "Pharmacokinetics of porcine insulin zinc suspension in diabetic dogs." *Journal of Small Animal Practice*. 1997. Vol 38, October: 434-438.

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vetsulin®
(porcine insulin zinc suspension)

Intervet

EXPECT MORE™

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