



**vetsulin**<sup>®</sup>  
(porcine insulin zinc suspension)

Questions? Visit [www.vetsulin.com](http://www.vetsulin.com)



## Vetsulin<sup>®</sup> and Canine Diabetes Mellitus

### THE PRODUCT

Vetsulin<sup>®</sup> (porcine insulin zinc suspension) is an aqueous suspension containing 40 IU per mL of highly purified porcine insulin consisting of 35 percent amorphous and 65 percent crystalline zinc insulin. As a lente insulin, Vetsulin is classified as an intermediate-acting insulin. Vetsulin has 2 peaks of insulin activity in dogs. The amorphous fraction provides quick activity, which peaks at approximately 4 hours following subcutaneous administration. The crystalline fraction is more slowly absorbed, providing a later peak of activity 11 hours post-injection. The impact of Vetsulin on blood glucose peaks at 4–8 hours post-injection and can last for 14–24 hours. Consequently, some dogs (approximately one-third) can be maintained on once-daily injections of Vetsulin.

*Vetsulin should not be used in dogs or cats known to have a systemic allergy to pork or pork products. Vetsulin 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 Vetsulin 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.*



## DIAGNOSING CANINE DIABETES MELLITUS

A preliminary diagnosis of diabetes mellitus based on clinical signs must be confirmed by blood and urine tests. Reference values for blood glucose range from 80–120 mg/dL (4.4–6.7 mmol/L) in dogs. The renal threshold is around 180 mg/dL (10 mmol/L). If the blood glucose concentration exceeds this threshold, glucose is excreted in the urine, which is indicative of diabetes.

### Presentation of a non-complicated diabetic dog

Two types of patients can be categorized as non-complicated:

1. Dogs presented to the veterinarian after the dog owner has noted the appearance of clinical signs without general deterioration—that is, no diabetic ketoacidosis (DKA). These cases are not emergencies, although dogs without cataracts should be treated diligently to try to avoid this complication.
2. Dogs that, after initial presentation with DKA and its successful treatment, are generally stable and without ketonuria.

### During consultation:

- ▶ Perform a thorough physical examination and weigh the dog.
- ▶ Conduct laboratory testing including complete blood count, urinalysis (including sediment examination), and serum biochemistry profile.
- ▶ Rule out hypothyroidism, renal failure, inflammatory bowel disease, pancreatitis, exocrine pancreatic insufficiency, hyperadrenocorticism, growth hormone excess or acromegaly, neoplasia, and hepatic disease.

### When health status is known and diabetes mellitus confirmed:

- ▶ Explain thoroughly to the dog owner what diabetes mellitus is, that achieving regulation may take time (up to 1–2 months), and what the implications are for the family. Make sure the dog owner understands the treatment involved, and that the dog should be able to live a happy, healthy life with consistent treatment. This is crucial, as complete cooperation of the owner is essential to the success of the treatment.
- ▶ Treat existing infections or other medical conditions. Many diseases will affect insulin metabolism.
- ▶ Introduce an appropriate diet.
- ▶ Begin treatment with Vetsulin® (porcine insulin zinc suspension).

## STARTING VETSULIN

Vetsulin therapy is ideally prescribed for newly diagnosed diabetic dogs or in cases where a change in insulin is indicated. Caution should be exercised when changing from one insulin product to another.

### In clinic:

- ▶ Weigh the dog. In the event of a fraction of a kilogram, round the body weight down rather than up. For example, a 12.9-kg dog should be dosed as a 12-kg dog. If the dog is grossly overweight, utilize the optimal body weight for calculating the starting dosage of Vetsulin.
- ▶ The starting dose is 0.5 IU/kg of body weight once daily concurrently with or right after a meal.
  - Once-daily injections are a good way for many dog owners to ease into the routine of diabetes management. This is preferable to having an overwhelmed client who sees euthanasia as the only viable option. After acclimating to the once-daily injections, the client is more likely to willingly accept twice-daily injections, if needed.
  - Remember that hyperglycemia does not kill dogs; however, hypoglycemia can be fatal. Overdosing of insulin can cause hypoglycemia.
  - The majority of dogs (approximately two-thirds) will require twice-daily Vetsulin injections.
- ▶ Keep the dog hospitalized for the day to verify that the starting dosage does not cause hypoglycemia.
- ▶ Instruct the dog owner about:
  - Injection technique
  - Parameters to monitor at home
  - Exercise recommendations
  - How to identify and treat hypoglycemia
  - Preferred diet and frequency of meals
- ▶ Discharge the dog to the owner's care for 1 week. This allows the patient and its owner to get used to injections. Alternatively, some practitioners may prefer to complete the initial regulation in clinic.

### At home, have the dog owner:

- ▶ Monitor and record water and food consumption.
- ▶ Monitor and record urine glucose and/or ketone bodies.
- ▶ Maintain starting dose and frequency of administration for the entire week unless there is evidence of hypoglycemia.



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## Monitoring and adjusting the dose

The pet should be returned for evaluation 6–7 days after starting Vetsulin.

- ▶ Obtain the owner's overall impression of the dog's progress.
- ▶ Reweigh the dog. Overall dosage of Vetsulin should be modified for significant weight gains or losses.
- ▶ A blood glucose curve should be evaluated to determine if regulation is achieved.
- ▶ Adjustments in dose based on the glucose curve evaluation should be in increments of 10 percent. For example, if a dog is currently receiving 12 IU twice daily and has a blood glucose curve that indicates inadequate regulation, the dose should be increased 10 percent or 1 IU.
- ▶ Additional adjustments in dose should be made no more frequently than every 5–7 days.
- ▶ Once regulated on Vetsulin, the dog should be rechecked every 2–4 months.



## VETSULIN: HANDLE WITH CARE

Vetsulin, like many other insulin preparations, is a suspension. The active ingredients in Vetsulin are present in the precipitate and in the clear supernatant. 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. If required, the product should be gently mixed to maintain a homogeneous, uniformly milky suspension before use. Clumps or white particles can form in insulin suspensions: do not use the product if visible clumps or white particles persist after shaking thoroughly.

Vetsulin vials should be stored upright in the refrigerator to avoid crystallization around the stopper. Once the vial is opened, use contents within 42 days of first vial puncture and maintain a temperature of 25°C (77°F) or cooler.

In addition, dog owners should be advised not to reuse insulin syringes. One of the main concerns is the potential for bacterial contamination and secondary infection. Also, the silicon coating inside the syringe may contaminate the insulin vial with silicon, resulting in a white precipitate forming in the vial, which may interfere with the biological activity of the insulin.

## VETSULIN: 40 IU/mL CONCENTRATION

Vetsulin, from Merck Animal Health, is the first registered veterinary insulin for the treatment of diabetes mellitus in dogs. Vetsulin is presented in a 10 mL glass vial at a concentration of 40 IU per mL of suspension. To avoid dosing errors when administering Vetsulin to dogs, it is important to use a U-40 syringe.

### **USE OF A SYRINGE OTHER THAN A U-40 SYRINGE WILL RESULT IN INCORRECT DOSING.**

As this potential situation can be fatal, it is strongly advised to educate dog owners to purchase both Vetsulin and the U-40 syringes from your veterinary clinic.



**Technical Services:** 1-800-224-5318. If you have a product issue, please be prepared to share the lot number and expiration date of the Vetsulin bottle in use.

# vetsulin®

(porcine insulin zinc suspension)

129347 R3

NADA 141-236, Approved by FDA

## 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 40 IU
(35% amorphous and 65% crystalline)
Zinc (as 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 and cats with diabetes mellitus.

## DOSE AND ADMINISTRATION

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

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. Clumps or white particles can form in insulin suspensions; do not use the product if visible clumps or white particles persist after shaking thoroughly. 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.

Always provide the Owner Information Sheet with each prescription.

## Dogs

The initial recommended vetsulin® dose is 0.5 IU insulin/kg body weight. Initially, this dose should be given once daily concurrently with, or right after a meal.

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 each be 25% less than the once daily dose required to attain an acceptable nadir. For example, if a dog receiving 20 units of vetsulin® once daily has an acceptable nadir but inadequate duration of activity, the vetsulin® dose should be changed to 15 units twice daily.

The veterinarian should re-evaluate the dog at appropriate intervals and adjust the dose based on clinical signs, urinalysis results, and glucose curve values until adequate glycemic control has been attained. 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.

## Cats

The initial recommended dose in cats is 1 to 2 IU per injection. The injections should be given twice daily at approximately 12 hour intervals. For cats fed twice daily, the injections should be given concurrently with, or right after each meal. For cats fed *ad libitum*, no change in feeding schedule is needed. The veterinarian should re-evaluate the cat at appropriate intervals and adjust the dose based on clinical signs, urinalysis results, and glucose curve values until adequate glycemic control has been attained. Further adjustments in dosage may be necessary with changes in the cat's diet, body weight, or concomitant medication, or if the cat develops concurrent infection, inflammation, neoplasia, or an additional endocrine or other medical disorder.

## CONTRAINDICATIONS

Dogs and cats 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:** Owners should be advised to observe for signs of hypoglycemia (see Owner Information Sheet). 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 in pets that are difficult to regulate (e.g., hyperadrenocorticism in dogs and hyperthyroidism in cats).

## 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 prevent 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 studies, dogs and cats received various medications while being treated with vetsulin® including antimicrobials, antivirals, antifungals, antihistamines, analgesics, anesthetics/tranquilizers, diuretics, bronchodilators, corticosteroids (cats), NSAIDs, thyroid hormone supplementation, hyperthyroid medication (methimazole), internal and external parasitides, anti-emetics, dermatological topical treatments and oral supplements, ophthalmic preparations containing antimicrobials and antiinflammatories, and various vaccines. No medication interactions were reported. This drug was not studied in dogs receiving corticosteroids.

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

**Use in puppies and kittens:** The safety and effectiveness of vetsulin® in puppies and kittens has not been evaluated.

## ADVERSE REACTIONS

### Dogs

In the field effectiveness and safety study, 66 dogs were treated with vetsulin®. Sixty-two dogs were included in the assessment of safety. Hypoglycemia (defined as blood glucose < 50 mg/dL) 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.

### Cats

In a field effectiveness and safety study, safety data was reported for 78 cats receiving vetsulin®. Hypoglycemia (defined as blood glucose < 50 mg/dL) was reported in 61 cats (88 total incidences). Fifteen of the occurrences (involving 13 cats) were associated with clinical signs described as lethargy, diarrhea, decreased appetite/anorexia, vomiting, and hypothermia. One cat had seizures following accidental overdosing by the owner and again during the subsequent dose adjustment period. The cat responded to supportive therapy and had no further hypoglycemic episodes. In all cases of hypoglycemia, the clinical signs resolved following symptomatic treatment and/or dose adjustment. Polyneuropathy was reported in 4 cats. Two injection site reactions were reported: one as a mildly thickened subcutaneous tissue reaction and the second as a mild bruising.

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 cats: vomiting, lethargy, diarrhea, decreased appetite/anorexia, pancreatitis, dermal events, respiratory disease, urinary tract disorder, renal disease, dehydration, weight loss, polydipsia, polyuria, behavioral change, and ocular discharge/conjunctivitis. In a smaller field effectiveness and safety study, 14 cats were treated with vetsulin®. Hypoglycemia was reported in 6 cats (8 total occurrences). Lethargy not associated with hypoglycemia was reported in 4 cats (6 total occurrences). 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 cats: foul odor to stool, diarrhea, dull coat, rapid, shallow breathing, stiff gait in rear, gallop rhythm, and pruritus with alopecia. During the 1998-2007 period, the following adverse events in 50 cats treated with porcine insulin zinc suspension were reported to Intervet International and Intervet Inc: Death, seizures, lack of effectiveness/dysregulation, hypoglycemia, allergic or skin reaction, lethargy, vomiting/diarrhea, injection pain, hyperthermia, nystagmus, PUPD, and abnormal behavior. To report suspected adverse drug experiences, call Merck at 1-800-224-5318. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or <http://www.fda.gov/AnimalVeterinary>

## GENERAL PHARMACOLOGY

vetsulin® is a mixture of amorphous and crystalline insulin resulting in immediate and prolonged insulin activity. In dogs, vetsulin® may show two peaks of activity. In a laboratory study, 12 healthy adult Beagles were administered vetsulin® at a dose of 0.5 IU/kg. The onset of activity varied from 0.5 to 2 hours; the time to peak activity varied from 1 to 10 hours; and the duration of activity varied from 10 to 24 hours. In diabetic dogs, vetsulin® has two peaks of activity following subcutaneous administration (the first occurs at 2 to 6 hours and the second at 8 to 14 hours) (1). The duration of activity varies between 14 and 24 hours (1).

In cats, vetsulin® has a single peak of activity. In a laboratory study, 12 healthy adult cats were administered vetsulin® at a dose of 0.5 IU/kg. The onset of activity varied from 0.5 to 2 hours; the time to peak activity varied from 2 to 6 hours; and the duration of activity varied from 8 to 24 hours. In diabetic cats, the peak activity following subcutaneous administration of vetsulin® occurs between 1.5 and 8 hours (2), and the duration of activity varies between 8 and 12 hours (2).

The peak(s) of activity, duration of activity, and dose required to adequately control diabetic signs vary between individuals and may vary in the same individual from day to day. The time ranges should only be considered as initial guidelines.

## EFFECTIVENESS

### Dogs

A total of 66 client-owned dogs were enrolled in and 53 completed the effectiveness and safety field study. The dogs 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. 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. 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.

### Cats

A total of 85 client-owned cats (53 males and 25 females—all neutered) of various breeds were enrolled in a 60 day field effectiveness and safety study with continued use up to Day 180. Seven cats were removed from the study prior to the Day 7 evaluation. The remaining cats ranged in age from 3 to 17.5 years and in weight from 1.9 to 10.8 kg. Seventy-two cats completed the study to Day 60 and 66 cats completed to Day 180. The cats were started on vetsulin® at an initial dose of 1 to 2 IU insulin twice daily. Scheduled evaluations occurred at Days 7, 14, 30, 60, and 180. Dose adjustments were allowed at and between the evaluations. Effectiveness was based on blood glucose curve mean, blood glucose nadir and improvement in clinical signs. Blood glucose curve means decreased from 394 mg/dL on Day 0 to 217 mg/dL on Day 60. The mean blood glucose nadir decreased from 343 mg/dL on Day 0 to 146 mg/dL on Day 60. Fourteen client-owned cats (10 males and 4 females—all neutered) of various breeds were enrolled in a 60 day effectiveness and safety field study. The cats ranged in age from 5 to 14 years and in weight from 3.40 to 6.97 kg. Twelve cats completed the study. The cats were started on vetsulin® at an initial dose of 1 to 2 IU insulin twice daily. Scheduled evaluations occurred at Days 7, 14, 30, and 60. Dose adjustments were allowed at and between the evaluations. The blood glucose curve means decreased from 354 mg/dL on Day 0 to 162 mg/dL on Day 60. The mean blood glucose nadir decreased from 321 mg/dL on Day 0 to 99 mg/dL on Day 60.

## HOW SUPPLIED

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

## STORAGE CONDITIONS

Store in an upright position under refrigeration at 2° to 8° C (36° to 46° F). Do not freeze. Protect from light. Use contents within 42 days of first vial puncture.

Additional information about vetsulin® and diabetes mellitus can be found at [www.vetsulin.com](http://www.vetsulin.com)

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Summit, NJ 07901

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## References

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