A DOG OWNER’S GUIDE.

Vetsulin® can help your diabetic dog lead a healthy, normal life.

For more information about Vetsulin® (porcine insulin zinc suspension) and diabetes mellitus in dogs, visit www.vetsulin.com.
Your dog has diabetes mellitus.

It can be a shock to learn that your dog has diabetes. Fortunately, diabetes in dogs can be managed successfully with insulin therapy, diet, and exercise. Your veterinarian can help make this possible with Vetsulin® (porcine insulin zinc suspension).

WHAT IS DIABETES MELLITUS?

During digestion, carbohydrates in your dog’s food are converted into various sugars, including glucose. Glucose is absorbed into the blood and provides energy to the body’s cells.

However, glucose can’t enter most cells without insulin, a hormone produced in the pancreas. When the pancreas produces little or no insulin, glucose cannot enter the body’s cells and accumulates in the blood. The result is diabetes mellitus. Simply put, diabetes results from a shortage of insulin.

YOUR DOG CAN LIVE A HEALTHY LIFE WITH DIABETES!

In general, diabetes can’t be cured. The good news is that, with some changes in your dog’s care and daily doses of Vetsulin, your dog will most likely be able to lead a normal, healthy life.

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.
Vetsulin®—just what your diabetic dog needs.

Vetsulin® (porcine insulin zinc suspension) is the only FDA-approved insulin for dogs, and it has been used successfully to treat dogs for more than 20 years worldwide.* You can take comfort in knowing that Vetsulin is the closest thing to a dog’s own insulin.

Your veterinarian will determine the dose that’s right for your dog and will teach you everything you need to know about administering the injection and monitoring your dog’s blood glucose level. Based on blood glucose levels, your veterinarian will adjust the dose until the correct dose is established. This time period can vary from 1 week to 1 or 2 months.

Look ahead with optimism.

Although Vetsulin is not a cure for diabetes, it can help control or eliminate many of the signs associated with the disease (such as excessive thirst, urination, and weight loss) and prevent development of life-threatening complications. The response to Vetsulin varies from dog to dog but can be quite dramatic. In most dogs, improvement can be seen within a few days.

If Vetsulin is not given as directed, signs of diabetes will return, and complications may develop. Once stabilized on insulin, most dogs are able to lead a happy, healthy life.

The life expectancy of dogs on insulin can be similar to that of other healthy dogs when diabetes is well managed.

MAKING SMALL CHANGES FOR THE BETTER.

Your veterinarian may ask you to take the following actions to help manage your dog’s diabetes:

- Change the times, amounts, and brand of food you feed your dog
- Ask family and friends to join you in eliminating extra dog treats
- Monitor your dog’s exercise, keeping it regular and routine
- Monitor your dog’s blood and urine glucose

PROGESTERONE, DIABETES, and your female dog.

As part of the treatment, your veterinarian will recommend that you have your dog spayed. That’s because one of the female sex hormones, progesterone, can interfere with the normal action of insulin. In order to remove the source of progesterone, spaying your diabetic female dog is essential.

*Vetsulin is sold as Caninsulin® outside of the US.
Avoiding possible complications.

The most common side effect experienced with Vetsulin® (porcine insulin zinc suspension) therapy or other insulin preparations is low blood sugar, also called hypoglycemia. When untreated, hypoglycemia can be fatal. Fortunately, knowing its causes can help you avoid unnecessary occurrences of hypoglycemia.

- Giving too much insulin
- Missing or delaying food
- Change in food, diet, or amount fed
- Increase in exercise
- Infection or illness
- Change in the body's need for insulin
- Adrenal, pituitary, or thyroid gland diseases or progression of liver or kidney disease
- Interaction with other drugs

SIGNS OF HYPOGLYCEMIA may occur suddenly and can include:

- Weakness
- Depression
- Behavioral changes
- Muscle twitching
- Anxiety
- Seizures
- Coma
- Death

What to do if hypoglycemia occurs.

IF YOUR DOG IS CONSCIOUS:

1. Rub about 1 tablespoon of corn syrup on your dog’s gums.
2. When your dog is able to swallow, feed the dog its usual meal.
3. Contact your veterinarian.

IF YOUR DOG IS UNCONSCIOUS OR HAVING A SEIZURE:

This is a medical emergency. CONTACT YOUR VETERINARIAN.

IN THE MEANTIME:

1. Treat your dog immediately. Do not delay treatment.
2. If your dog is unconscious, pour a small amount of corn syrup onto your finger and rub it onto your dog’s gums.
3. The sugar is absorbed very quickly (1–2 minutes), after which your dog should respond.
4. Do not pour the solution directly in your dog’s mouth, since there is a risk it could be inhaled into the lungs.
5. Once your dog has responded and is sitting up, feed it a small amount of its usual meal.
6. When your dog is stabilized, immediately take him/her to your veterinarian for evaluation.
vetsulin®

(porcine insulin zinc suspension)

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**

**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 during formulation 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 ovariohysterectomized. 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, antibiotics, analgesics, anesthetics/tranquilizers, diuretics, bronchodilators, corticosteroids (cats), NSAIDs, thyroid hormone supplementation, hyperthyroid medication (methimazole), internal and external parasiticides, anti-emetics, dermatological topical treatments and oral supplements, ophthalmic preparations containing antimicrobials and anti-inflammatories, 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 not 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 hepatopathypancreatitis, 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 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

Distributed by: Intervet Inc (d/b/a Merck Animal Health)
Summit, NJ 07901

Made in Germany
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References

For more information on diabetes and Vetsulin, please also see the Owner Information Sheet included in the Vetsulin packaging.