

IT'S ABOUT TIME TO MAKE THINGS EASIER FOR YOUR FELINE DIABETIC PATIENTS

INTRODUCTORY OFFER – Valid through March 31, 2010*

PLACE YOUR QUALIFYING ORDER TODAY

**Each vial of PROZINC purchased includes
a Diabetes Care Kit at no charge**

- Minimum purchase of 3 vials on one invoice

ADDITIONAL VALUE FOR YOUR CLIENTS

For a limited time, you can give away our free PROZINC Diabetes Care Kit with each PROZINC purchase.

The kit contains:

- **U-40 syringes (100 count)** to help ensure your clients administer the correct dose with the correct syringe.
- **PROZINC pet owner brochure** to reinforce your instructions and recommendations.
- **Syringe disposal container** to help pet owners properly dispose of needles and syringes.

KEEPS YOUR CLIENTS COMING BACK

- Veterinary exclusive offer
- Give this kit free to clients with each purchase of PROZINC from your hospital
- Approximate clinic value \$15

*Introducing the
PROZINC Diabetes Care Kit
FREE with qualifying order*



**Contact your *Boehringer Ingelheim* or preferred distributor representative
today to place your qualifying order of PROZINC.**

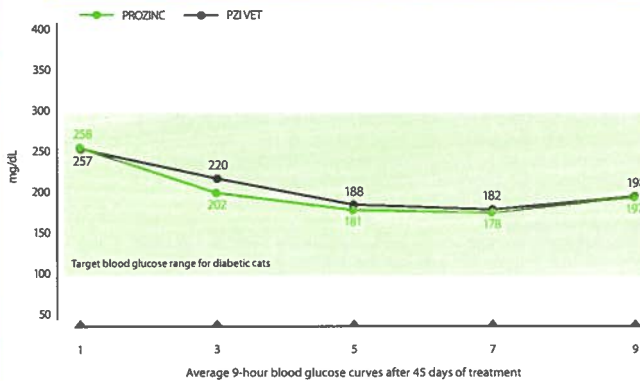
www.ProZinc.us
www.BI-Vetmedica.com

*Or while supplies last

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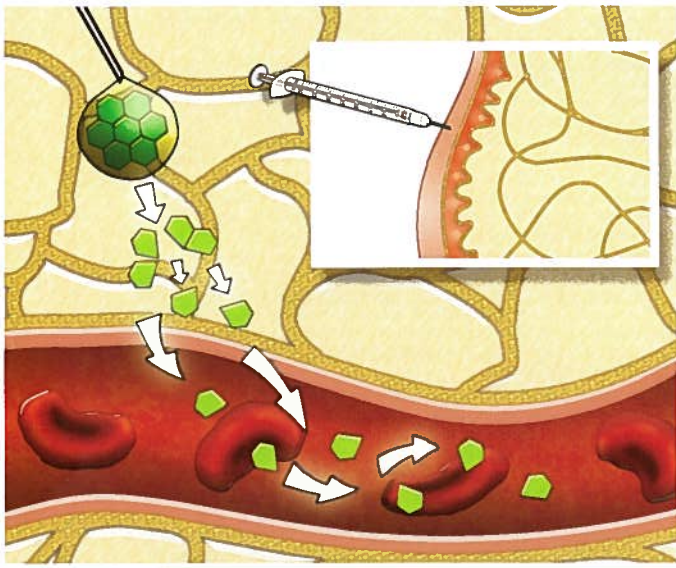
NEW
ProZinc™
(protamine zinc recombinant human insulin)

Comparison of mean 9-hour glucose curves of cats receiving PROZINC¹ vs. PZI VET²



*The analysis compares data generated in a 2009 pre-approval efficacy study for PROZINC with data generated in a 2001 efficacy study performed for PZI VET using virtually identical study protocols. The PZI VET product, which was also marketed by IDEXX, has been discontinued.

PROZINC delivers long-acting glycemic control



IMPORTANT SAFETY INFORMATION

As a class, the use of any insulin when regulating a diabetic cat may be associated with side effects. The most common side effect reported in field studies was hypoglycemia. This is usually mild (lethargy, weak, trembling, uncoordinated, groggy, dazed), but may be serious and life-threatening (seizures, coma). If side effects occur, cat owners should contact their veterinarian immediately. Cats should be evaluated for pre-existing conditions and currently prescribed medications prior to treatment with PROZINC. Routine monitoring (blood parameters such as glucose and fructosamine and clinical signs) is essential to maintain a regulated cat. PROZINC insulin is contraindicated during episodes of hypoglycemia. Please refer to the reverse side for complete product information.

¹Data on file. St. Joseph, MO: Boehringer Ingelheim Vetmedica.

²Extrapolated from Nelson RW, Lynn RC, Wagner-Mann CC, et al. Efficacy of protamine zinc insulin for treatment of diabetes mellitus in cats. *JAVMA*. 2001;218(1):38-42.

³Norsworthy G, Lynn R, Cole C. Preliminary study of protamine zinc recombinant insulin for the treatment of diabetes mellitus in cats. *Vet Ther*. 2009;10(1-2):24-28.

⁴Nelson RW, Henley K, Cole C, et al. Field safety and efficacy of protamine zinc recombinant human insulin for treatment of diabetes mellitus in cats. *J Vet Intern Med*. 2009;23:787-793.

⁵Nelson RW. Disorders of the Endocrine Pancreas. In: Nelson RW, Couto CG, eds. *Small Animal Internal Medicine*. 4th ed. St. Louis, MO: Mosby Elsevier; 2008:764-802.

⁶Plumb DC. *Plumb's Veterinary Drug Handbook*. 5th ed. Hoboken, NJ: Wiley-Blackwell; 2005:412-418.

⁷Ganong WF. *Ganong's Review of Medical Physiology*. 22nd ed. New York, NY: McGraw-Hill Medical Publishing; 2005:333-355.

⁸FOI for NADA 141-297. (PROZINC)

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PZI VET is a trademark or a registered trademark of IDEXX Laboratories, Inc. in the United States and/or other countries.
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IT'S ABOUT TIME

INTRODUCING **ProZinc**[™] (protamine zinc recombinant human insulin)

A study published in 2009 (Norsworthy, Lynn, Cole) found that PZIR (PROZINC) provides glycemic control that is comparable to that of PZI VET[®] (protamine zinc insulin) when used at the same dose and dosing interval.³

THE PREDICTABLE GLYCEMIC CONTROL OF A PROTAMINE ZINC INSULIN

- The same consistent performance veterinarians experience with PZI VET is now available in a recombinant human protamine zinc insulin: new PROZINC.^{3,4}

THE FIRST LONG-ACTING PROTAMINE ZINC INSULIN FDA-APPROVED SPECIFICALLY FOR CATS

- Protamine zinc insulin formulations are classified as long-acting with a typical duration of effect in the cat of 10-14 hours.⁵ In PROZINC insulin, zinc and the protein protamine are combined to form insulin hexamers to slow their dissociation into monomers that can be absorbed and used by the body.^{6,7}

FELINE SPECIFIC

- PROZINC was designed for cats and is backed by clinical data⁸ from the largest prospective study in diabetic cats.

THE RELIABLE SUPPLY OF A HUMAN RECOMBINANT INSULIN

- The human recombinant technology of PROZINC is not subject to raw material sourcing constraints of older, animal-source insulin products.

**Confidently recommend PROZINC,
the right choice for diabetic cats.**



ProZinc™

(protamine zinc recombinant human insulin)

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

Description: ProZinc™ insulin is a sterile aqueous protamine zinc suspension of recombinant human insulin.

Each mL contains:

recombinant human insulin	40 International Units (IU)
protamine sulfate	466 mg
zinc oxide	0.088 mg
glycerin	16.00 mg
dibasic sodium phosphate, heptahydrate	3.78 mg
phenol (added as preservative)	2.50 mg
hydrochloric acid	1.63 mg
water for injection (maximum)	1005 mg
pH is adjusted with hydrochloric acid and/or sodium hydroxide.	

Indication: ProZinc (protamine zinc recombinant human insulin) is indicated for the reduction of hyperglycemia and hyperglycemia-associated clinical signs in cats 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 CATS ONLY.

ProZinc insulin should be mixed by gently rolling the vial prior to withdrawing each dose from the vial. Using a U-40 insulin syringe, the injection should be administered subcutaneously on the back of the neck or on the side of the cat.

Always provide the Cat Owner Information Sheet with each prescription.

The initial recommended ProZinc dose is 0.1 – 0.3 IU insulin/pound of body weight (0.2 – 0.7 IU/kg) every 12 hours. The dose should be given concurrently with or right after a meal. The veterinarian should re-evaluate the cat at appropriate intervals and adjust the dose based on both clinical signs and glucose nadirs until adequate glycemic control has been attained. In the effectiveness field study, glycemic control was considered adequate if the glucose nadir from a 9-hour blood glucose curve was between 80 and 150 mg/dL and clinical signs of hyperglycemia such as polyuria, polydipsia, and weight loss were improved.

Further adjustments in the 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: ProZinc insulin is contraindicated in cats sensitive to protamine zinc recombinant human insulin or any other ingredients in the ProZinc product. ProZinc insulin is contraindicated during episodes of hypoglycemia.

Warnings: User Safety: For use in cats only. Keep out of the reach of children. Avoid contact with eyes. In case of contact, immediately flush eyes with running water for at least 15 minutes. Accidental injection may cause 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 Cat 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, if indicated, the dosage adjusted.

Any change in insulin should be made cautiously and only under a veterinarian's supervision. Changes in insulin strength, manufacturer, type, species (human, animal) 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 other endocrinopathies in diabetic cats 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 to prevent associated complications. Overdosage can result in profound hypoglycemia and death. Progestogens, certain endocrinopathies and glucocorticoids can have an antagonistic effect on insulin activity. Progestogen and glucocorticoid use should be avoided.

Reproductive Safety: The safety and effectiveness of ProZinc insulin in breeding, pregnant, and lactating cats has not been evaluated.

Use in Kittens: The safety and effectiveness of ProZinc insulin in kittens has not been evaluated.

Adverse Reactions: Effectiveness Field Study

In a 45-day effectiveness field study, 176 cats received ProZinc insulin. Hypoglycemia (defined as a blood glucose value of < 50 mg/dL) occurred in 71 of the cats at various times throughout the study. Clinical signs of hypoglycemia were generally mild in nature (described as lethargic, sluggish, weak, trembling, uncoordinated, groggy, glassy-eyed or dazed). In 17 cases, the veterinarian provided oral glucose supplementation or food as treatment. Most cases were not associated with clinical signs and received no treatment. One cat had a serious hypoglycemic event associated with stupor, lateral recumbency, hypothermia and seizures.

All cases of hypoglycemia resolved with appropriate therapy and if needed, a dose reduction.

Three cats had injection site reactions which were described as either small, punctate, red lesions; lesions on neck; or palpable subcutaneous thickening. All injection site reactions resolved without cessation of therapy.

Four cats developed diabetic neuropathy during the study as evidenced by plantigrade stance. Three cats entered the study with plantigrade stance, one of which resolved by Day 45. Four cats were diagnosed with diabetic ketoacidosis during the study. Two were euthanized due to poor response to treatment. Five other cats were euthanized during the study, one of which had hypoglycemia. Four cats had received ProZinc insulin for less than a week and were euthanized due to worsening concurrent medical conditions.

The following additional clinical observations or diagnoses were reported in cats during the effectiveness field study: vomiting, lethargy, diarrhea, cystitis/hematuria, upper respiratory infection, dry coat, hair loss, ocular discharge, abnormal vocalization, black stool, and rapid breathing.

Extended Use Field Study

Cats that completed the effectiveness study were enrolled into an extended use field study. In this study, 145 cats received ProZinc insulin for up to an additional 136 days. Adverse reactions were similar to those reported during the 45-day effectiveness study and are listed in order of decreasing frequency: vomiting, hypoglycemia, anorexia/poor appetite, diarrhea, lethargy, cystitis/hematuria, and weakness. Twenty cats had signs consistent with hypoglycemia described as: sluggish, lethargic, unsteady, wobbly, seizures, trembling, or dazed. Most of these were treated by the owner or veterinarian with oral glucose supplementation or food; others received intravenous glucose. One cat had a serious hypoglycemic event associated with seizures and blindness. The cat fully recovered after supportive therapy and finished the study. All cases of hypoglycemia resolved with appropriate therapy and if needed, a dose reduction.

Fourteen cats died or were euthanized during the extended use study. In two cases, continued use of insulin despite anorexia and signs of hypoglycemia contributed to the deaths. In one case, the owner decided not to continue therapy after a presumed episode of hypoglycemia. The rest were due to concurrent medical conditions or worsening of the diabetes mellitus.

To report suspected adverse reactions, or to obtain a copy of the Material Safety Data Sheet (MSDS), call 1-866-638-2226.

Information for Cat Owners: Please refer to the Cat Owner Information Sheet for more information about ProZinc insulin. ProZinc insulin, like other insulin products, is not free from adverse reactions. Owners should be advised of the potential for adverse reactions 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 most common adverse reaction observed is hypoglycemia. Signs may include: weakness, depression, behavioral changes, muscle twitching, and anxiety. In severe cases of hypoglycemia, seizures and coma can occur.

Hypoglycemia can be fatal if an affected cat 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 therapy is appropriate, or if alternative therapy should be considered.

Effectiveness: A total of 187 client-owned cats were enrolled in a 45-day field study, with 176 receiving ProZinc insulin. One hundred and fifty-one cats were included in the effectiveness analysis. The patients included various purebred and mixed breed cats ranging in age from 3 to 19 years and in weight from 4.6 to 20.8 pounds. Of the cats included in the effectiveness analysis, 101 were castrated males, 49 were spayed females, and 1 was an intact female.

Cats were started on ProZinc insulin at a dose of 0.1-0.3 IU/lb (0.2-0.7 IU/kg) twice daily. Cats were evaluated at 7, 14, 30, and 45 days after initiation of therapy and the dose was adjusted based on clinical signs and results of 9-hour blood glucose curves on Days 7, 14, and 30.

Effectiveness was based on successful control of diabetes which was defined as improvement in at least one blood glucose variable (glucose curve mean, nadir, or fructosamine) and at least one clinical sign (polyuria, polydipsia, or body weight). Based on this definition, 115 of 151 cases (76.2%) were considered successful. Blood glucose curve means decreased from 415.3 mg/dL on Day 0 to 203.2 mg/dL by Day 45 and the mean blood glucose nadir decreased from 407.9 mg/dL on Day 0 to 142.4 mg/dL on Day 45. Mean fructosamine values decreased from 505.9 µmol/L on Day 0 to 380.7 µmol/L on Day 45.

Cats that completed the effectiveness study were enrolled in an extended use field study. The mean fructosamine value was 342.0 µmol/L after a total of 181 days of ProZinc therapy.

How Supplied: ProZinc insulin is supplied as a sterile injectable suspension in 10 mL multidose vials. Each mL of ProZinc product contains 40 IU recombinant human insulin.

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

Manufactured for:
Boehringer Ingelheim Vetmedica, Inc.
St. Joseph, MO 64506 U.S.A.

Manufactured by:
AAI Pharma, Charleston, SC 29405

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