

**AAHA-RECOMMENDED  
AND FDA-APPROVED**

**ProZinc<sup>®</sup>**

(protamine zinc recombinant  
human insulin)

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**TRUSTED  
FELINE  
DIABETES  
CARE.**

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Make PROZINC<sup>®</sup> (protamine zinc  
recombinant human insulin) your  
first-line treatment for diabetic cats.






**UNIQUE**


# THE ONLY AAHA-RECOMMENDED AND FDA-APPROVED TREATMENT FOR FELINE DIABETES.


The 2018 AAHA Diabetes Management Guidelines recommend that veterinary professionals make every effort to USE VETERINARY FDA-APPROVED PRODUCTS and base their inventory-purchasing decisions on what product is most beneficial to the patient.<sup>1</sup>


**TWICE-DAILY DOSING OF PROZINC® (protamine zinc recombinant human insulin) DELIVERS PREDICTABLE GLYCEMIC CONTROL.<sup>2</sup>**


**U-40 SYRINGE IMPROVES SAFETY AND PRECISION.<sup>6</sup>**

 **PROZINC Delivers** 10–14 hour duration of effect (Glargine’s duration of effect curve can vary<sup>3</sup>)

 **Cats Require** 2 injections a day, 12 hours apart<sup>4,5</sup>

 **Easier** to read, for consistent dosing

 **Minimizes The Risk** of accidental over- or underdosing

 **More Accurate** and precise than U-100 syringes when administering small doses

**IMPORTANT SAFETY INFORMATION:** PROZINC is for use in cats and dogs only. 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 is essential to attain and maintain adequate glycemic control and to prevent associated complications. Overdosage can result in profound hypoglycemia and death. Progestogen and glucocorticoid use should be avoided. PROZINC insulin is contraindicated in cats during episodes of hypoglycemia and in cats sensitive to protamine zinc recombinant human insulin or any other ingredients in the PROZINC product. **For more information, please see enclosed full prescribing information for cats.**



**PROVEN**

## UNPARALLELED DATA DEMONSTRATES GLYCEMIC CONTROL IN DIABETIC CATS<sup>2</sup>

**76%**

of patients treated with PROZINC<sup>®</sup> (protamine zinc recombinant human insulin) achieved treatment success\* by day 45<sup>5</sup>

- 76% of cats demonstrated improvement in polydipsia
- 74% of cats demonstrated improvement in polyuria



Significant reductions in mean 9-hour post-injection blood glucose<sup>5</sup>



Significant reductions in mean serum fructosamine<sup>5</sup>



Significant increases in mean body weight, and improvement in body condition scores<sup>5</sup>

Diet change was not required to achieve treatment success<sup>5</sup>

Additional study findings<sup>5</sup>:

- 89% of cats had a good body condition score by day 45
- With extended use, glycemic control remained evident after 6 months of therapy with PROZINC, based on favorable fructosamine concentrations

\*Treatment success at Day 45 was based on documentation of stable or increasing body weight, achievement of good body condition, improvement in 9-hour mean blood glucose and/or serum fructosamine concentration, and owner-reported improvement in polyuria and polydipsia.

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# DEPENDABLE

## DELIVERS FAVORABLE REMISSION RATES AND RAPID GLYCEMIC CONTROL



Diabetic remission rate is independent of insulin formulation, and no single factor predicts remission.<sup>7</sup> However, cats that experience remission are more likely to have achieved rapid glycemic control<sup>7</sup>



PROZINC® (protamine zinc recombinant human insulin)'s rapid efficacy promotes conditions that favor remission<sup>8</sup> - In a field study, 76% of cats that received PROZINC achieved diabetic control in 45 days.



In a year-long, randomized trial comparing PROZINC and Glargine in recently-diagnosed diabetic cats, *remission rates were not significantly different between groups, and glycemic control was comparable<sup>9</sup>*



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## Package Insert for Cats

# ProZinc® (protamine zinc recombinant human insulin)

40 IU/mL

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

**Description:** PROZINC® is a sterile aqueous protamine zinc suspension of recombinant human insulin.

Each mL contains:

recombinant human insulin	40 International Units (IU)
protamine sulfate	0.466 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 ONLY.

DO NOT SHAKE OR AGITATE THE VIAL.

**PROZINC should be mixed by gently rolling the vial prior to withdrawing each dose from the vial.** Once mixed, PROZINC suspension has a white, cloudy appearance. Clumps or visible white particles can form in insulin suspensions; do not use the product if clumps or visible white particles persist after gently rolling 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 Client 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 is contraindicated in cats sensitive to protamine zinc recombinant human insulin or any other ingredients in PROZINC. PROZINC is contraindicated during episodes of hypoglycemia.

**Warnings: User Safety:** For use in cats and dogs 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 Client Information Sheet). Use of this product, even at established doses, has been associated with hypoglycemia. A cat 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:** Cats 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 is essential to attain and maintain adequate glycemic control and to prevent associated complications. Overdose can result in profound hypoglycemia and death.

Glucocorticoids, progestogens, and certain endocrinopathies can have an antagonistic effect on insulin activity. Glucocorticoid and progestogen use should be avoided.

The safety and effectiveness of PROZINC in breeding, pregnant, and lactating cats has not been evaluated.

The safety and effectiveness of PROZINC in kittens has not been evaluated.

### **Adverse Reactions: Effectiveness Field Study**

In a 45-day effectiveness field study, 176 cats received PROZINC. 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 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 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 drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim at 1-888-637-4251.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at [www.fda.gov/reportanimalae](http://www.fda.gov/reportanimalae).

**Information for Cat Owners:** Please refer to the Client Information Sheet for Cats for more information about PROZINC. PROZINC, 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. 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 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 is supplied as a sterile injectable suspension in 10 mL and 20 mL multi-dose vials. Each mL of PROZINC 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. **Use the 10 mL vial within 60 days of first puncture. Use the 20 mL vial within 80 days of first puncture.**

Approved by FDA under NADA # 141-297

### **Marketed by:**

Boehringer Ingelheim Animal Health USA Inc.  
Duluth, GA 30096

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Revised 08/2019

449986-01

# PARTNERS

## TAKE ADVANTAGE OF BENEFITS FOR YOUR PRACTICE AND EXCEPTIONAL PRODUCT SUPPORT FROM THE LEADERS IN FELINE INSULIN THERAPY:



**PROZINC® (protamine zinc recombinant human insulin) Diabetes Care Kits** that increase ease and convenience for clients and provide an easy way to properly dispose of used syringes and needles



**Educational Materials** provide feline-specific educational resources for your healthcare team



**Technical Support** from Professional Service Veterinarians and our on-call support team at **1-888-637-4251**

## FOR MORE INFORMATION

Contact your Boehringer Ingelheim representative.

<sup>1</sup> Behrend E, Holford A, Lathan P, Rucinsky R, Schulman R. 2018 AAHA diabetes management guidelines for dogs and cats. *J Am Anim Hosp Assoc.* 2018;54(1):1-21.

<sup>2</sup> PROZINC® (protamine zinc recombinant human insulin) [Freedom of Information Summary].

<sup>3</sup> Nelson RW. Disorders of the endocrine pancreas. In: Nelson RW, Cuoto CG, eds. *Essentials of Small Animal Internal Medicine*. 4th ed. St. Louis, MO: Mosby Elsevier; [https://books.google.com/books?id=s-TXrwyo-\\_YC&pg=PA787&lpg=PA787&dq=nelson+rw+disorders+of+the+endocrine+pancreas&source=bl&ots=Gb2nBqrlpb&sig=ACfU3U1H-3-OCFH9ajQMRJg\\_2CtldxGVQ&hl=en&sa=X&ved=2ahUKewjmveSjIKDnAhXA13IEHQ2IDhg4ChDoATABegQlChAB#v=onepage&q=nelson%20rw%20disorders%20of%20the%20endocrine%20pancreas&f=true/](https://books.google.com/books?id=s-TXrwyo-_YC&pg=PA787&lpg=PA787&dq=nelson+rw+disorders+of+the+endocrine+pancreas&source=bl&ots=Gb2nBqrlpb&sig=ACfU3U1H-3-OCFH9ajQMRJg_2CtldxGVQ&hl=en&sa=X&ved=2ahUKewjmveSjIKDnAhXA13IEHQ2IDhg4ChDoATABegQlChAB#v=onepage&q=nelson%20rw%20disorders%20of%20the%20endocrine%20pancreas&f=true/). Accessed January 28, 2020:764-802.

<sup>4</sup> Rucinsky R, Cook A, Haley S, Nelson R, Zoran DL, Poundstone M. AAHA diabetes management guidelines for dogs and cats. *J Am Anim Hosp Assoc.* 2010;46(3):215-224.

<sup>5</sup> Nelson 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.

<sup>6</sup> Borin-Crivellenti S, Bonagura JD, Gilor C. Comparison of precision and accuracy of U100 and U40 insulin syringes. 2014 ACVIM Forum Research Abstracts Program. *J Vet Intern Med.* 2014;28:1029.

<sup>7</sup> Gastelow R, Forcada Y, Graves T, et al. Systematic review of feline diabetic remission: separating fact from opinion. *Vet J.* 2014;202(2):208-21.

<sup>8</sup> PROZINC® Prescribing Information.

<sup>9</sup> Gastelow R, Scudder C, et al. One-year prospective randomized trial comparing efficacy of glargine and protamine zinc insulin in diabetic cats. Abstract format, ACVIM Proceedings, June 2017.