

Dudley—focused on discovering new worlds.

PROZINC—focused on Dudley.

No matter what your patients are focused on, PROZINC is the ideal insulin choice that meets their individual needs.

ProZinc[®]
(protamine zinc recombinant human insulin)



PROZINC is focused on treating feline

Achieving control with insulin.

Insulin, along with diet modification, is the mainstay of treatment for cats with clinical diabetes.¹

Insulin therapy goals¹



Reduce clinical signs



Achieve a good quality of life



Minimize complications

Appropriate treatment choices.

- Insulin must have an appropriate duration of action to avoid blood glucose level variation between doses
- Only 2 types of insulin have the desired duration for most cats:¹



Human protamine zinc insulin
Veterinary approved



Insulin glargine
Not veterinary approved

What about remission?

Diabetic cats sometimes experience remission.
Factors that can contribute to remission include:²

- Early diagnosis and the extent of beta cell damage
- Recognition and treatment of insulin-antagonistic diseases
- Recognition and treatment of underlying infection
- Effective insulin treatment
- Feeding an appropriate diet
- Blood glucose monitoring
- Duration of insulin therapy

Care and monitoring are still important for cats in remission because clinical signs can recur.

diabetes.

ProZinc[®]
(protamine zinc recombinant human insulin)



PROZINC puts the needs of cats first.

The ideal solution for all newly diagnosed diabetic cats.

- The ONLY AAHA-recommended **and** FDA-approved insulin for the first-line treatment of diabetic cats¹
- Offers predictable glycemic control and efficacy proven to improve clinical signs³
- Backed by the largest prospective study in diabetic cats to date⁴
- Supported by Boehringer Ingelheim Vetmedica, Inc. (BIVI)

“ I believe that we should be starting newly diagnosed cats on PROZINC. I think it gives them the best chance of eliminating clinical signs in a safe and healthy way. ”

— Richard E. Goldstein, DVM,
DACVIM, DECVIM-CA
Chief Medical Officer
The Animal Medical Center in New York City

Important Safety Information: PROZINC insulin, like other insulin products, is not free from adverse reactions. The most common reaction observed is hypoglycemia.

Jimmer - focused on soaring to new heights.

PROZINC - focused on Jimmer.

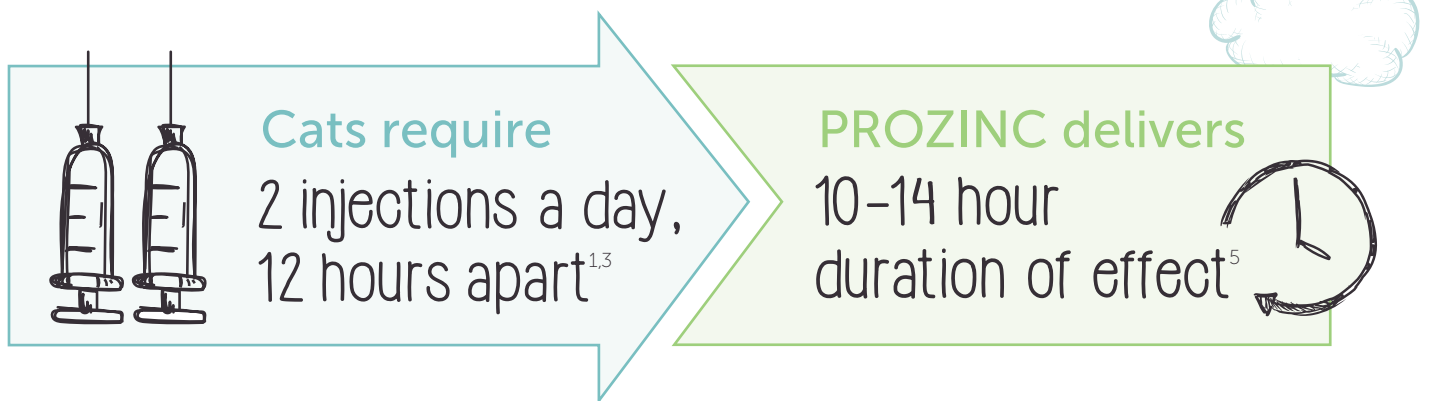


PROZINC is focused on details that ma

Features that are just right for cats.

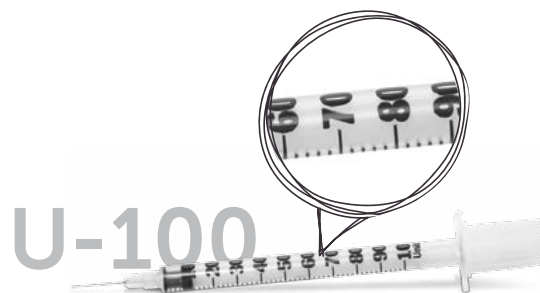
Appropriate duration of action for cats.¹

- PROZINC is a protamine zinc insulin (PZI), which has a typical duration of effect lasting 10–14 hours⁵



U-40 syringe for easier and more consistent dosing.

- Easier to read
- More accurate and precise than U-100 syringes⁶
- Less likely to result in clinically important over- or underdosing⁶



Make the difference.

ProZinc[®]
(protamine zinc recombinant human insulin)



The ideal choice over glargine.

Compared to glargine,
PROZINC gives you more

	PROZINC	Insulin glargine
FDA approved for cats	✓	
Appropriate duration of action in cats ¹	✓	✓
Recombinant insulin source	✓	✓
May induce remission	✓	✓
Easy-to-dose U-40 syringe	✓	
Product support from a veterinary pharmaceutical company	✓	
Pet owner and education tools available	✓	
Profitable for your practice	✓	
Diabetes Care Kit offered	✓	

“Glargine’s duration of effect isn’t long enough to maintain good control all day with just a single dose. But for many cats, it’s too long for twice-daily dosing.”

— Richard W. Nelson, DVM, DACVIM
Professor, Department of Medicine and Epidemiology
UC Davis School of Veterinary Medicine

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. Please refer to the package insert for complete product information.

PROZINC is focused on you and your patients.

BIVI provides unmatched support.

Helping you and your clients manage feline diabetes.



Veterinary-approved PROZINC gives you more control over patient care by driving business to your clinic instead of a human pharmacy



PROZINC Diabetes Care Kits make feline diabetes care easier for your clients by providing necessary supplies, such as U-40 syringes, a pet owner brochure, and a syringe disposal container



Feline-specific educational resources, including the PROZINC website (PROZINC.us), provide reliable and easy-to-access information for your healthcare team



Pet owner education materials and tools, including MyCatHasDiabetes.com, deliver valuable disease and treatment information to your clients



Technical support from Professional Service Veterinarians and our on-call support team (1-866-638-2226) provide assistance when you need it

“As a veterinarian, it’s really important to have that support from the company that makes the insulin. There are helplines you can call into, there’s a website [where] you can get a lot of advice and support. Those things are not available if you’re using human insulin.”

— J. Catharine Scott-Moncrieff, DVM, DACVIM, DECVIM-CA
Professor of Small Animal Internal Medicine
Purdue University College of Veterinary Medicine

Clifford—focused on reaching the top.

PROZINC—focused on Clifford.



ProZinc®

(protamine zinc recombinant human insulin)



NADA 141-297, Approved by FDA

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	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 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 Services Corp.
Charleston, SC 29405

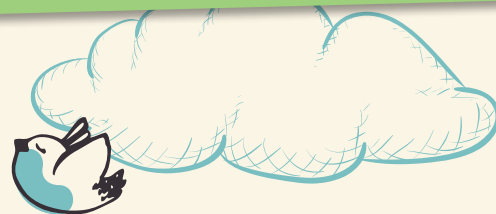
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PROZINC is focused on putting diabetic cats first.

- Proven efficacy to reduce clinical signs³
- Appropriate duration of action for cats^{1,5}
- The only veterinary insulin recommended by the AAHA for the first-line treatment of diabetic cats¹
- Unmatched product support, technical assistance, and resources from BIVI, the industry leader in feline insulin therapy



“For cats that are newly diagnosed with diabetes mellitus, I recommend starting with PROZINC insulin.”

— J. Catharine Scott-Moncrieff, DVM, DACVIM, DECVIM-CA
Professor of Small Animal Internal Medicine
Purdue University College of Veterinary Medicine

Contact your BIVI territory manager to make PROZINC your first choice for your newly diagnosed feline diabetic patients.

BIVI Technical Support: 1-866-638-2226
PROZINC.us
BI-Vetmedica.com



Important Safety Information: For use in cats 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 is contraindicated in cats during episodes of hypoglycemia and in cats sensitive to protamine zinc recombinant human insulin or any other ingredient in the PROZINC product.

References: 1. Rucinsky R, Cook A, Haley S, et al. AAHA diabetes management guidelines for dogs and cats. *J Am Anim Hosp Assoc.* 2010;46(3):215–224. 2. Ford SL. Feline diabetic remission: Is it the cat or the insulin? *Vet Pract News.* 2010;42–44. 3. 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. 4. ProZinc® (protamine zinc recombinant human insulin) [Freedom of Information Summary]. St. Joseph, MO: Boehringer Ingelheim Vetmedica, Inc.; 2009. 5. 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; 2008:764–802. 6. 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.