

## 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 <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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## Client Information Sheet for Cats

# ProZinc® (protamine zinc recombinant human insulin)

### 40 IU/mL

This summary contains important information about PROZINC. You should read this information before you start giving your cat PROZINC and review it each time the prescription is refilled. This sheet is provided only as a summary and does not take the place of instructions from your veterinarian. Talk to your veterinarian if you do not understand any of this information or if you want to know more about PROZINC.

#### What is PROZINC?

PROZINC is an aqueous protamine zinc suspension of recombinant human insulin that is used to reduce high blood sugar (hyperglycemia) in cats with diabetes mellitus. A veterinarian must prescribe PROZINC for your cat. **PROZINC should be given to cats only.** Keep out of reach of children. Seek medical attention immediately if you accidentally inject yourself with PROZINC.

#### What is diabetes mellitus?

Diabetes mellitus occurs when a cat has insufficient levels of, or an abnormal response to, insulin. The low insulin levels may result in high blood sugar (hyperglycemia) that could produce the following changes in your cat:

- Increased thirst
- High levels of sugar (glucose) in the urine (glucosuria)
- Weight loss
- Increased appetite
- Increased urination
- Weakness in the back legs

#### What kind of results can I expect when my cat is on PROZINC for diabetes mellitus?

Although PROZINC is not a cure for diabetes mellitus, it can help reduce the levels of sugar (glucose) in the blood, which can help alleviate the clinical signs.

#### What should I discuss with my veterinarian before giving PROZINC?

Talk to your veterinarian about:

- The signs of diabetes mellitus you have observed in your cat (for example, increased thirst and urination).
- The importance of proper PROZINC storage, handling, and administration techniques (for example, how to gently roll the vial prior to each use, the proper appearance of product after gently rolling, how to fill the U-40 syringe with the proper amount of insulin, and where and how to inject the insulin).
- The importance of maintaining your cat under the same conditions for diet, exercise, environment, etc.
- The importance of follow-up visits for testing to determine if dose adjustments of PROZINC are necessary.

Tell your veterinarian about:

- Any side effects your cat has had when receiving other insulin products.
- Any medical problems or allergies that your cat has now or has had in the past.
- All medications that you are giving your cat or plan to give your cat, including those you can get without a prescription.
- If your cat is pregnant, nursing, or if you plan to breed your cat.

#### What are the possible side effects that may occur in my cat during PROZINC therapy?

PROZINC, like other drugs, may cause side effects. Serious side effects can occur with or without warning. Please contact your veterinarian immediately if you think your cat has a medical problem or side effect from PROZINC therapy. The most common insulin-related side effect is low blood sugar (hypoglycemia). Signs of low blood sugar (hypoglycemia) can occur suddenly and may include:

- Weakness
- Depression, lethargy, sluggishness
- Staggering gait
- Behavioral changes
- Muscle twitching
- Seizures, convulsions
- Coma
- Death

#### What actions do I take if my cat shows signs of low blood sugar (hypoglycemia)?

- If your cat is unconscious or having a seizure, this is a medical emergency. Take your cat to the veterinarian immediately.
- If your cat is conscious, rub approximately 1 tablespoon of corn syrup or honey on your cat's gums. When it is able to swallow, give corn syrup or honey by mouth until your cat is alert enough to eat. Feed the usual meal and contact your veterinarian.

#### When should my cat not be given PROZINC?

Do not give your cat its prescribed dose of PROZINC if it:

- Is experiencing an episode of low blood sugar (hypoglycemia). Common causes for low blood sugar include excessive doses of insulin, failure to eat, strenuous exercise, changes in the body's need for insulin, diabetes-inducing disease or drug effects.
- Is not eating or is vomiting.
- Is sensitive to protamine zinc recombinant human insulin or any other ingredients in PROZINC.
- Do not give your cat its prescribed dose of PROZINC if you see clumps or visible white particles in the vial after gently rolling.

#### How should I give PROZINC to my cat?

PROZINC should be given with or right after a meal.

**Give PROZINC with U-40 syringes only.** Use of a syringe other than a U-40 syringe will result in incorrect dosing. Gently roll the vial until the PROZINC has a uniformly cloudy, white appearance. If there are clumps or visible white particles in the vial after gently rolling, do not use the PROZINC and call your veterinarian. PROZINC should be given according to your veterinarian's instructions. Your veterinarian will tell you what amount of PROZINC is right for your cat and instruct you on techniques for administration.

#### Can PROZINC be given with other medications?

PROZINC can be given with other medications, but the dose may need to be adjusted due to the medication resulting in either increased or decreased insulin requirements. Tell your veterinarian about all medications you have given your cat in the past, and any medications that you are planning to give with PROZINC. This should include medications that you can get for your cat without a prescription. Your veterinarian may want to ensure that all of your cat's medications can be given together.

#### What should I do if I inject more than the prescribed amount of PROZINC?

Contact your veterinarian immediately and, if your veterinarian is not available, seek other veterinary advice at once.

#### What should I do if my cat receives less than the prescribed dose, or I miss an injection?

- Contact your veterinarian as soon as possible for advice on your cat's next dose.
- If you cannot reach your veterinarian and your cat is eating and acting normally, give your cat the usual dose at the next regularly scheduled injection time.

#### How should I store PROZINC?

PROZINC should be stored 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.**

#### What else should I know about PROZINC?

This sheet provides a summary of information about PROZINC. If you have any questions or concerns about the product or diabetes mellitus, talk to your veterinarian.

As with all prescribed medications, PROZINC should only be given to the cat for which it is prescribed and for the condition for which it was prescribed.

It is important to periodically discuss your cat's response to PROZINC at regular checkups that may include blood glucose monitoring. Your veterinarian will best determine if your cat is responding as expected and should continue receiving PROZINC.

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