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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.

Cat Owner Information about ProZinc® (protamine zinc recombinant human insulin)

ProZinc insulin is indicated for the reduction of hyperglycemia and hyperglycemia-associated clinical signs in cats with diabetes mellitus.

This summary contains important information about ProZinc insulin. You should read this information before you start giving your cat ProZinc insulin 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 insulin.

What is ProZinc insulin?

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

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 glucose that could produce the following changes in your cat:

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

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

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

What should I discuss with my veterinarian before giving ProZinc insulin?

Talk to your veterinarian about:

- The signs of diabetes mellitus you have observed (for example, increased thirst and urination).
- The importance of proper insulin storage and administration techniques (for example, how to gently roll the vial prior to each use, 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 the 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 insulin 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 insulin, like other drugs, may cause some 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 glucose (hypoglycemia). Signs of hypoglycemia may occur suddenly and can include:

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

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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What actions do I take if my cat shows signs of 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 insulin?

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

- Is experiencing an episode of low blood glucose (hypoglycemia). Common causes for hypoglycemia 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 product.

How should I give ProZinc insulin to my cat?

Give ProZinc insulin with U-40 syringes only. Use of a syringe other than a U-40 syringe will result in incorrect dosing. ProZinc insulin should be given according to your veterinarian's instructions. Your veterinarian will tell you what amount of ProZinc insulin is right for your cat and instruct you on techniques for administration.

Can ProZinc insulin be given with other medications?

ProZinc insulin 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 insulin. This should include medications that you can get 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 insulin?

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 insulin?

ProZinc insulin should be stored in an upright position under refrigeration at 36-46°F (2-8°C). Do not freeze. Protect from light.

What else should I know about ProZinc insulin?

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

As with all prescribed medications, ProZinc insulin 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 insulin 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 insulin.

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