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 PRESENCE 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 study field, 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 (DNA vs human-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 suppleent. Most cases were not associated with clinical signs and received no treatment. One cat had a severe 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; 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 elected 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 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 purebreds and mixed breed cats ranging in age from 3 to 19 years and in weight from 4.5 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/kg (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 (polypnea, 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 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

© 2019 Boehringer Ingelheim Animal Health USA Inc. All rights reserved. US-PET-0697-2021

Boehringer Ingelheim

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.
Clinical pathology: The only change seen in complete blood count, serum chemistry and urinalysis results was an increase in the blood glucose curve values and shape, nadir, and fructosamine until adequate glycemic control has been attained. The effectiveness field study, glycemic control was considered adequate if the glucose nadir from a 9-hour blood glucose curve was between 40 and 125 mg/dL, the maximum blood glucose was < 300 mg/dL, and clinical signs that paralleled such as polyuria, polydipsia, or weight loss were improved.

Use of this product, even at established doses, has been associated with hypoglycemia. A dog with signs of hypoglycemia did not resolve with supportive care. Hypoglycemia without clinical signs was defined as two consecutive blood glucose curve values < 60 mg/dL unaccompanied by clinical signs.

Diabetic ketoacidosis and pancreatitis: Eleven dogs were diagnosed with diabetic ketoacidosis. Four of these 11 dogs died or were euthanized, one after one dose of PROZINC. Twenty-one dogs were diagnosed with pancreatitis. Seven of these 21 dogs died or were euthanized due to complications of pancreatitis. Four dogs had concurrent diabetic ketoacidosis and pancreatitis, three of which died or were euthanized. Not all the dogs were considered related to PROZINC.

Deaths: Thirty-six (36) dogs died or were euthanized, six of which were possibly related to PROZINC. One dog died from recurrent episodes of pancreatitis, and one died after developing severe vomiting and diarrhea followed by a seizure. Four dogs euthanized: one developed severe pancreatitis and azotemia, one had recurrent episodes of pancreatitis and diabetic ketoacidosis, and two for lack of effectiveness.

To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet, contact Boehringer Ingelheim at 1-888-637-4275.

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/animaldrugs.