PROZINC® Care Kits for Cats and Dogs

We know managing a diabetic pet may be challenging for pet owners. One factor that contributes to the complexity is dosing imprecision, specifically when small volumes of insulin are required. Safely disposing of syringes and needles daily can also become a challenge. To help, Boehringer Ingelheim is proud to provide Diabetes Care Kits as part of the PROZINC® (protamine zinc recombinant human insulin) family of resources available to our customers. With the Diabetes Care Kit, pet owners can rest assured that they are using the appropriate syringes and needles, and are able to dispose of them safely, and have the right tools to pair with PROZINC at home.

WHAT’S INCLUDED

Kits come in both 0.33 cc and 1 cc dosing formats and include:

- **100 U-40 syringes**
  U-40 syringes are designed specifically for administration of PROZINC® insulin (per label) in dogs and cats. Use of other syringes such as U-100 can lead to incorrect dosing. The use of U-40 syringes allows correct administration of small doses of insulin. Overall, compared to U-100, U-40 are less likely to result in clinically important over- or under-dosing. These results favor the use of U-40 syringes for administration of small doses of insulin. The kit is designed to last each client about 50 or 80 days, depending on dosing instructions— the same amount of time it takes to finish a vial of PROZINC.

- **A syringe disposal container**
  Ensuring safe disposal of used syringes and needles.

CLINIC BENEFITS

- **Increases engagement with pet owners**
  Clients with diabetic pets will need to re-purchase new vials of PROZINC and syringes several times per year, giving you the opportunity for frequent interactions and Care Kit sales.

- **Increases ease and convenience for clients**
  Provides your clients the appropriate and easy way to administer PROZINC and dispose of used syringes and needles.

- **Helps ensure the right dose every time**
  Ensures the appropriate syringe size and needle gauge are being used so that dosing is as accurate as possible.

PET OWNER BENEFITS

- **Safely stores used needles and syringes**
- **Clear and easy-to-read calibrations on syringes**
- **Precise and consistent dosing; less waste of insulin**
- **The right number of syringes for the amount of PROZINC purchased**
- **Opportunities to discuss their pet’s progress with the veterinarian**

Scan the QR code to the right for more information on diabetes in cats and dogs.

To order PROZINC® Care Kits, contact your Boehringer Ingelheim Sales Representative.

IMPORTANT SAFETY INFORMATION: PROZINC® (protamine zinc recombinant human insulin) is 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. Use of a syringe other than U-40 will result in incorrect dosing. For more information, please see full prescribing information.
All cases of hypoglycemia resolved with appropriate therapy and if needed, a dose reduction.

Favorable effects developed diabetic neuropathy during the study as evidenced by plantargrade stance. Three cats entered this study with plantargrade 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 some 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.

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. Like other insulin products, PROZINC 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 hypoglycemia (Somogy 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 purebreds 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 male. 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 other variable. A cat was considered improved if fasting blood glucose was less than 150 mg/dL for at least 8 of 10 test days. A total of 181 days of PROZINC therapy. The mean fructosamine value was 342.0 μmol/L after a total of 181 days of PROZINC therapy. The mean fructosamine value was 342.0 μmol/L after a total of 181 days of PROZINC therapy.

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In a 182-day field study, 276 dogs received PROZINC. The most common adverse reactions were hyperglycemia and hyperglycemia-associated clinical signs in dogs with diabetes mellitus.

Injection site reactions: Seven dogs had injection site reactions, including observations of thickened skin, swelling, bumps at the injection site, and redness. All injection site reactions resolved without cessation of PROZINC therapy. Reaction to the injection, including vocalization, was observed in four dogs. Hyperglycemia: There were 80 hyperglycemic episodes recorded during the study with some dogs experiencing more than one episode; 37 episodes were associated with clinical signs in 24 dogs. 40 episodes were without clinical signs in 27 dogs, and 3 were with unknown signs in 2 dogs. Clinical signs of hyperglycemia varied and included seizure, collapse, ataxia, staggering, trembling, twitching, shaming, disorientation, lethargy, weakness, and vomiting. In some dogs required treatment. Dehydration and some dogs died or were euthanized due to shock. Four dogs were euthanized when the hyperglycemia did not resolve with supportive care. Hypoglycemia without clinical signs was defined as two consecutive blood glucose curve values ≤ 40 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 of these dogs were diagnosed with a low blood glucose. Seven of the 11 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 deaths 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 were euthanized: one developed severe pancreatitis and azotemia, one had recurrent episodes of pancreatitis and diabetic ketoacidosis, and two for lack of effectiveness. Location: Boehringer Ingelheim at 1-888-537-4251.

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/reportanimalmed.

Table 1. Adverse reactions seen in the safety population (276 dogs)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Number and Percentage</th>
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<tbody>
<tr>
<td>Anorexia (anorexia, decreased appetite, inappetence, and not eating)</td>
<td>28 (10.1%)</td>
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<tr>
<td>Hypoglycemia with clinical signs</td>
<td>24 (8.9%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>21 (7.6%)</td>
</tr>
<tr>
<td>Seizures</td>
<td>16 (5.8%)</td>
</tr>
<tr>
<td>Shaking/trembling/twitching</td>
<td>13 (4.7%)</td>
</tr>
<tr>
<td>Ataxia (ataxia, balance problem, stumbling gait)</td>
<td>11 (4.0%)</td>
</tr>
<tr>
<td>Diarrhea (diarrhea, loose stools, and loose stools)</td>
<td>9 (3.3%)</td>
</tr>
<tr>
<td>Disorientation/confusion</td>
<td>9 (3.3%)</td>
</tr>
<tr>
<td>Weakness</td>
<td>8 (2.9%)</td>
</tr>
<tr>
<td>Restlessness/anxiety/ agitation</td>
<td>6 (2.2%)</td>
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<tr>
<td>Cataract</td>
<td>5 (1.8%)</td>
</tr>
<tr>
<td>Panting (panting and tachypnea)</td>
<td>5 (1.8%)</td>
</tr>
<tr>
<td>Hematuria</td>
<td>4 (1.5%)</td>
</tr>
</tbody>
</table>

Clinical Pathology: The only change seen in complete blood count, serum chemistry, and urinalysis results was an elevation in mean cholesterol at Day 182 (432.6 mg/dL, normal range 131-345 mg/dL) compared to Day 1 (333.7 mg/dL).

Table 2. Pharmacodynamics of three dosing groups

<table>
<thead>
<tr>
<th>Dose Group</th>
<th>Onset of Action</th>
<th>Time to nadir</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 IU/kg at a single site</td>
<td>1 to 2 hours</td>
<td>6 to 16 hours</td>
<td>16 to 24 hours</td>
</tr>
<tr>
<td>0.8 IU/kg at a single site</td>
<td>0.5 to 1 hours</td>
<td>6 to 16 hours</td>
<td>16 to 24 hours</td>
</tr>
<tr>
<td>0.8 IU/kg divided at three sites</td>
<td>1 to 10 hours</td>
<td>8 to 20 hours</td>
<td>18 to 24 hours</td>
</tr>
</tbody>
</table>

Information for Dog Owners: Please refer to the Client Information Sheet for Dogs 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 may include hypoglycemia, insulin antagonist/resistance, rapid insulin metabolism, insulin-induced hypoglycemia (Somogy Effect), and local or systemic reactions. The most common adverse reaction observed was hypoglycemia. Signs may include weakness, depression, behavioral changes, muscle twitching, and ataxia. If hypoglycemia occurs, ataxia, hypothermia, and vomiting may occur. If hypoglycemia can occur. Hyperglycemia can be fatal if an affected dog 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 276 client-owned dogs were enrolled in an 84-day field study followed by a 98-day extended-use phase with 276 dogs receiving PROZINC. The dogs included various purebred and mixed breed dogs ranging in age from 2 to 16 years and in weight from 3.3 to 123 pounds. There were 128 neutered males, 8 intact males, 134 spayed females and 6 intact females. Two hundred forty-two dogs (224) were included in the effectiveness analysis. Dogs were started on PROZINC at a dose of 0.2-0.5 IU/kg once daily.

Dogs were evaluated at 7, 14, 21, 28, 63, and 84 days after initiation of therapy. The dose was adjusted based on clinical signs and results of 9-hour blood glucose curves on Days 1, 14, 21, 28, 42, 63 and 84. Effectiveness was based on successful control of diabetes which was defined as improvement in at least one laboratory variable (blood glucose curve mean, blood glucose curve nadir, or fructosamine) and at least one clinical sign (polyuria, polydipsia, or weight loss). Based on this definition, 162 of 224 cases (72%) were considered successful.

How Supplied: PROZINC is supplied as a sterile injectable suspension in 10 mL and 20 mL multi-dose vials. Each mL of PROZINC contains 4 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.

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