Boehringer Ingelheim

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Now available in 10 & 20 ml vials

Canine diabetes mellitus management guide

ProZinc®
(protamine zinc recombinant human insulin)

*All dogs should be started on once-daily dosing; twice-daily dosing may be considered if insufficient improvement in diabetic control is observed after 4–6 weeks.

Experience
optimal management of diabetes

ProZinc® has a prolonged duration of effect of approximately 18 to 24 hours in dogs.[1–4] This allows:

1. Optimal insulin dosing

- Convenient **ONCE-DAILY** dosing is now possible for most dogs[1–5]
- ProZinc® should be started once daily regardless of whether the patient is insulin-naive or transitioning from another insulin[1,2]

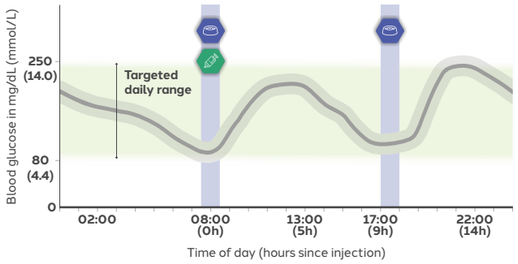
2. Flexible feeding options

- Accommodates for graze-feeding of meals and low carbohydrate snacks, which can help to reduce glucose peaks and troughs in dogs fed twice daily
- Pet owners have more options when it comes to the feeding regimen

3. Monitoring based mainly on clinical signs

- If clinical signs are improving blood glucose will be within the appropriate range for most of the day. Well-controlled dogs may have a normal blood glucose at the time of insulin administration (Fig. 1)
- Dose adjustments should be based primarily on clinical signs, supported by laboratory parameters where needed
- Dog owners should be encouraged to record presence/absence of clinical signs in the ProZinc® Home Care Journal

Figure 1. Example canine blood glucose curve



- This is an example of the biphasic curve that may be expected when dogs are well-controlled on once-daily ProZinc® with twice-daily feeding[4]
- The timing and value of the glucose peaks and nadirs are dependent on the timing of insulin administration and feeding
- A different-shaped curve may be seen if the dog is a graze-feeder

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Diagnosis
and initial management

Diagnosis of diabetes mellitus is based on[6]:

- **Clinical signs** – polyuria (PU), polydipsia (PD), polyphagia and weight loss. If the patient is anorexic, test for diabetic ketoacidosis (DKA)*
- **Laboratory results** – hyperglycaemia with glucosuria on at least two occasions. Fructosamine may be supportive in diagnosis and future management

Additional data to help detect concurrent disease includes[6]:

- Haematology
- Biochemistry
- Full urine analysis, including culture
- Blood pressure

Management with ProZinc® 1

- **Insulin-naive dogs:** Start with **0.5 IU/kg once-daily dosing**
- **Pretreated dogs:** Start **between 0.5 and 1.0 IU/kg once daily** even if the dog has previously been dosed twice daily with another insulin
- Treat concurrent inflammatory diseases (e.g. urinary tract infection, dental disease, skin disease, pancreatitis), which could interfere with the action of ProZinc®
- Taking the time to explain all aspects of diabetes management (including the importance of regular and accurate dosing) and to demonstrate preparing and administering ProZinc® helps familiarise owners with diabetic care
- Informing owners that the ProZinc® starting dose may need to be titrated helps owners to understand that it might take some time to achieve stabilisation
- The ProZinc® Dog Owner Brochure helps to familiarise owners with diabetic care and the ProZinc® Home Care Journal supports monitoring of clinical signs, exercise and weight.

Feeding

- Dogs should be fed twice daily – give the first meal with or just before their ProZinc® injection and the second meal 9–10 hours later
- Some dogs may be hungry between mealtimes. Graze-feeding of measured portions is acceptable, and owners should not hesitate to give hungry dogs a small low carbohydrate snack

*If DKA is present, hospitalisation and emergency treatment are indicated.

Monitoring

General principles

Good control is based on[6]:

- **Improved clinical signs** (reduction in PU/PD and polyphagia, with maintenance/gaining of weight and muscle mass)
- No signs of hypoglycaemia or diabetes mellitus progression

Reassessments are recommended every 7–14 days until control is achieved, 1 month later and then every 3–4 months.

Evaluation of good control with ProZinc® is based primarily on improved clinical signs.

Cynthia R. Ward, VMD, PhD, DACVIM, College of Veterinary Medicine, University of Georgia

Monitoring blood glucose

Blood glucose curves are generally not required during the stabilisation phase with ProZinc®. Continuous glucose monitoring (CGM) or a 14-hour blood glucose curve may be helpful to check for short duration of action of insulin or suboptimal dosing if there are signs of hypoglycaemia, if clinical signs persist beyond 6 weeks, or if the dose reaches 1.5 IU/kg. It is recommended that factors such as compliance problems, activity or diet change and concurrent disease are ruled out prior to carrying out CGM or a blood glucose curve.

If monitoring **serum fructosamine** is planned, the value at diagnosis would serve as a baseline. Repeating fructosamine is deemed appropriate once the patient has been on the same insulin dose for 2 to 3 weeks and then every second week until assessed as good control by improved clinical signs and a satisfactory fructosamine level (e.g. <400 µmol/L).

Home blood glucose monitors can be used to check for hypoglycaemia if the dog is showing suggestive clinical signs or to inform decisions on whether the dog should be given ProZinc® when inappetent. Owners should be discouraged from taking daily blood glucose measurements as this creates unnecessary stress for the dog. In case home blood glucose monitoring is carried out and owners report occasional non-symptomatic hypoglycaemia (blood glucose <4.4 mmol/L), it is often not necessary to change the ProZinc® dose, but do advise the owner to feed their dog a snack at that time.

Reassessments

First reassessment

- Timing is based on owner confidence with injections – usually 7–14 days but earlier if owner requires additional support
- Ask the owner to demonstrate drawing up insulin and the injection procedure using sterile water for injection or saline
- Weigh the patient and ask about presence of clinical signs (PU/PD, appetite)
- Dose adjustments are probably not necessary at this stage—be patient with your patient

Further reassessments

- Continue reassessments and dose titration based on clinical signs every 7 to 14 days until there is good control (see dose adjustment section)
- Ask about presence of clinical signs of both hyper- and hypoglycaemia
- Weigh the patient and assess muscle mass
- Check for compliance issues and concurrent diseases, which could interfere with insulin action

Week 6 reassessment

- Ask about presence of clinical signs of both hyper- and hypoglycaemia
- Weigh the patient and assess muscle mass
- If clinical signs persist:
  - Rule out compliance problems, activity or diet change
  - Check for concurrent diseases, which could be causing insulin resistance (e.g. hyperadrenocorticism, hypothyroidism and inflammatory conditions such as bacterial infections and pancreatitis)
  - Consider CGM (e.g. with Freestyle Libre®) or a 14-hour blood glucose curve to rule out short duration of action of insulin and suboptimal dose
- No clinical signs: reassess in 1 month

3–4 monthly reassessments of the stabilised patient

- Assess history for presence/absence of clinical signs
- Weigh the patient, assess muscle mass and assess for concurrent disease
- Consider fructosamine if history is unreliable or incomplete

*The **ProZinc® Home Care Journal** helps you at each visit to assess improvement or worsening of clinical signs and changes in routine.*

Dose adjustments

General principles

- A decision to increase dose should be based on **continued presence of clinical signs** of hyperglycaemia
- As ProZinc® has a prolonged duration of action, dose changes can take a while to impact clinical signs. For this reason, **dose should be increased no more frequently than weekly**
- It may take 6 weeks or sometimes longer for good control, so **be patient with your patient** and do not be tempted to increase the dose too quickly

Dosing increments

- If clinical signs are not improved, **increase insulin dose by up to 25%**, no more frequently than weekly

What if the patient is difficult to control?

If clinical signs persist:

- Rule out compliance problems, activity or diet change
- Check for concurrent diseases, which could be causing insulin resistance
- Consider CGM (e.g. with Freestyle Libre®) or a 14-hour blood glucose curve to rule out short duration of action of insulin and suboptimal dose

If CGM or blood glucose curve shows:

- **Short duration of insulin action** (blood glucose rising above 13.9 mmol/L <14 hours after insulin injection and no subsequent decrease in blood glucose prior to next insulin injection): Switch the dog to twice-daily dosing, reducing the dose per injection by one third (e.g. if the current dose is 12 IU once daily, change to 8 IU twice daily)
- **Symptomatic hypoglycaemia** (blood glucose <4.4 mmol/L with clinical signs such as lethargy, weakness, ataxia, seizures) or **Somogyi phenomenon***: Reduce insulin dose by 50% or restart stabilisation at 0.5 IU/kg

***For additional technical advice**, refer to the ProZinc® package insert or consult your Boehringer Ingelheim Technical Veterinarian.*

*Somogyi phenomenon is also known as a hypoglycaemic-induced hyperglycaemic event.

Canine Diabetes Mellitus Management Flowchart

Step 1: Diagnosis

DIABETES MELLITUS

Clinical signs

- Polyuria, polydipsia, polyphagia, weight loss

Laboratory results

- Hyperglycaemia with glucosuria on 2 occasions *or*
- Hyperglycaemia with glucosuria and high serum fructosamine

CONCURRENT DISEASE

Minimum database

- Haematology and biochemistry
- Urine analysis including culture
- Blood pressure

Step 2: Initial Management

Initiate ProZinc® therapy **AT A DOSE OF 0.5–1.0 IU/KG** every 24 hours

Insulin-naive dogs: Start with 0.5 IU/kg
Pretreated dogs: Start between 0.5 and 1.0 IU/kg

Feed appropriate diet
Regular exercise

Treat concurrent disease

Step 3: Monitoring

REASSESSMENT

Assess for presence of clinical signs

- History, physical examination, body weight (initially every 1–2 weeks)

± Laboratory results

- Fructosamine (every second reassessment)
- Blood glucose (BG) curve/continuous glucose monitoring (CGM)

Step 4: Dose Adjustment

PERSISTENT CLINICAL SIGNS

Increase dose by up to 25%

If clinical signs >42 days or dose >1.5 IU/kg, rule out:

- Compliance problems
- Activity or diet change
- Concurrent disease
- Short duration of action of insulin
  - If <14 hours, switch to twice-daily dosing, reducing dose per injection by one third
- Somogyi phenomenon
  - If confirmed, reduce dose by 50% or restart stabilisation at 0.5 IU/kg

RECHECK: 1–2 weeks

NO CLINICAL SIGNS

Continue current ProZinc® dose

RECHECK: 1 month then every 3–4 months

Encourage use of home care journal

SIGNS OF HYPOGLYCAEMIA

Reduce dose by 50%

- Treat hypoglycaemia
- Administer next dose when BG >250 mg/dL (14 mmol/L)

RECHECK: 1 day then 1 week

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Manage your patients' diabetes with ProZinc® (protamine zinc recombinant human insulin)

Achieve control of diabetes mellitus with ProZinc® in dogs and cats:

- The recommended insulin for cats[6,7]
- With ProZinc® up to 83% of dogs can be successfully treated with once-daily dosing[3]*

ProZinc®—available in 10 and 20ml vials.

References: 1. ProZinc® Summary of Product Characteristics (SPC). European Medicines Agency website. Available at: https://www.ema.europa.eu/en/documents/product-information/prozinc-epar-product-information_en.pdf. Accessed December 14, 2021. **2.** PROZINC® Freedom of Information Summary: Canine. NADA 141-297. February 8, 2019. **3.** CVMP assessment report for type II variation for ProZinc® (EMEA/V/C/002634/II/0015). European Medicines Agency website. Available at: https://www.ema.europa.eu/en/documents/variation-report/prozinc-v-c-2634-ii-0015-epar-assessment-report-variation_en.pdf. Accessed December 14, 2021. **4.** Ward CR, Winhall M, Kroh C, et al. Assessment of once daily dosing with ProZinc® insulin in diabetic beagle dogs. Proceedings of the 2021 ACVIM Forum; June 9–12, 2021; Virtual. Abstract EN12. **5.** Ward CR, Christiansen K, Li J, et al. Field efficacy and safety of protamine zinc recombinant human insulin in 276 dogs with diabetes mellitus. *Domest Anim Endocrinol.* 2021;75:106575. **6.** Behrend E, Holford A, Lathan P, et al. AAHA diabetes management guidelines for dogs and cats. *J Am Anim Hosp Assoc.* 2018;54:1–21. **7.**Sparkes A, Cannon M, Church D, et al. ISFM consensus guidelines on the practical management of diabetes mellitus in cats. *J Feline Med Surg.* 2015;17:235-250.

ProZinc® (protamine zinc insulin) ProZinc 40 IU/ml suspension for injection for cats and dogs. Prescription medicine. AQ10AC01. Indication: For the treatment of diabetes mellitus in cats and dogs to achieve reduction of hyperglycaemia and improvement of associated clinical signs. Contraindications: Do not use for the acute management of diabetic ketoacidosis. Do not use in cases of hypersensitivity to the active substance or to any of the excipients. The safety and efficacy of ProZinc in breeding, pregnant and lactating animals has not been evaluated. Use only according to the benefit-risk assessment by the responsible veterinarian. In general, insulin requirements during pregnancy and lactation might be different due to a change in the metabolic state. Therefore, close glucose monitoring and veterinary supervision is advised. Dose and administration route: Subcutaneous use. If the animal owner is to administer the product, suitable training/advice should be provided by the prescribing veterinarian before using for the first time. Cats: The initial recommended dose is 0.2 to 0.4 IU insulin/kg bodyweight every 12 hours. Dogs: For initiation of treatment, the recommended dose is 0.5 to 1.0 IU insulin/ kg bodyweight once daily every morning (approx. every 24 h). Shelf life: Unopened: 3 years, after opening immediate packaging: 60 days. This text is based on the summary of product characteristics dated 2019-11-07. For more information see www.fass.se. For prices: See www.fass.se. Boehringer Ingelheim Animal Health Nordics A / S, Box 467, 201 24 Malmö, tel. 040 23 34 00, fax 040 97 27 50, www.vetportal.seBoehringer Ingelheim Animal Health Nordics A/S, Box 467, 201 24 Malmö, tel. 040 23 34 00, fax 040 97 27 50, www.vetportal.se

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