

# PROZINC<sup>®</sup> HELPS KEEP THEM BOTH IN BALANCE

A guide to managing diabetes in cats and dogs with ProZinc<sup>®</sup>



# CONTENTS OF THIS GUIDE

This booklet is intended as a reference guide to help you manage diabetes in cats and dogs with ProZinc®. If you have any questions about ProZinc® or would like discuss any specific cases, please do not hesitate to contact our Technical Services team (contact details are on page 17 and the back cover).

PAGE

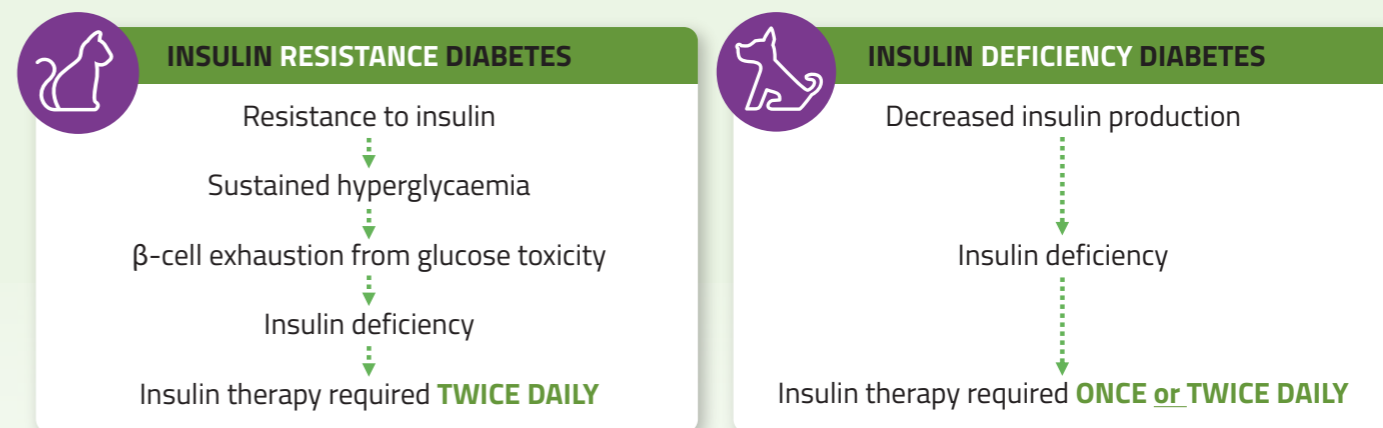
- 3** **DIABETES IN CATS & DOGS: A REFRESHER**
- 4** **PROZINC®: A LONGER-ACTING INSULIN**
- 6** **PROZINC® IN CATS**
- 8** **PROZINC® IN DOGS**
- 10** **HOW TO SUCCESSFULLY USE PROZINC®**
  1. Make a confident diagnosis, then start ProZinc®
  2. Monitor the patient
  3. Reassess regularly
  4. Adjust the ProZinc® dose gradually for optimal control
- 16** **PROZINC® STABILISATION FLOWCHART**
- 17** **OWNER AND VETERINARY SUPPORT**
- 18** **NOTES**



# DIABETES IN CATS & DOGS: A REFRESHER

## Cats and dogs get different forms of diabetes

It is now well-recognised that **cats tend to get insulin resistance diabetes** (similar to type 2 diabetes in humans), whereby their pancreas produces insulin, but their body is resistant to it. This results in sustained hyperglycaemia, and makes the beta-cells of the pancreas work harder to produce more insulin which eventually become exhausted from glucose toxicity. Insulin levels then become deficient, which means when they reach this point, insulin therapy is always necessary, despite them originally being insulin resistant. Cats generally metabolise insulin quickly, **so normally require insulin twice daily**.

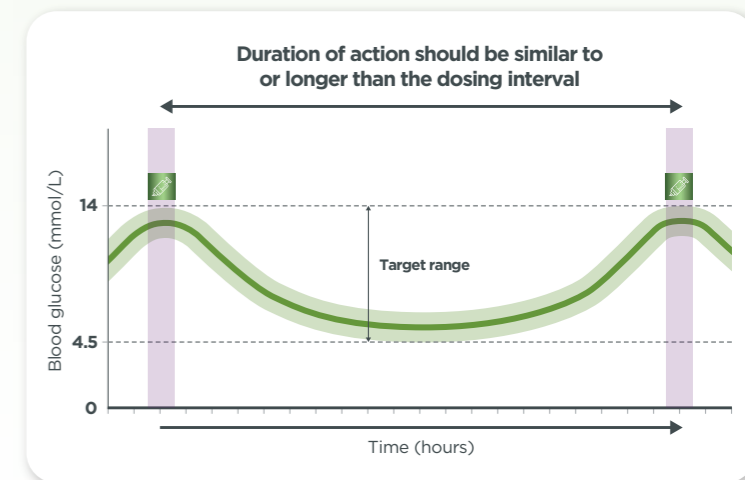


Unlike cats, **dogs generally get insulin deficiency diabetes**, which is similar to type 1 diabetes in humans. Their pancreas does not produce enough insulin which can be for a variety of reasons, but essentially this means **dogs always need ongoing insulin therapy once or twice daily** since they metabolise insulin more slowly than cats.

## Principles of managing diabetes in cats and dogs with insulin

The goal of managing diabetes in cats and dogs is to control clinical signs using an insulin regime that fits into the owner's daily life, whilst avoiding hypoglycaemia and other diabetic complications (e.g. ketosis, ketoacidosis, cataracts).

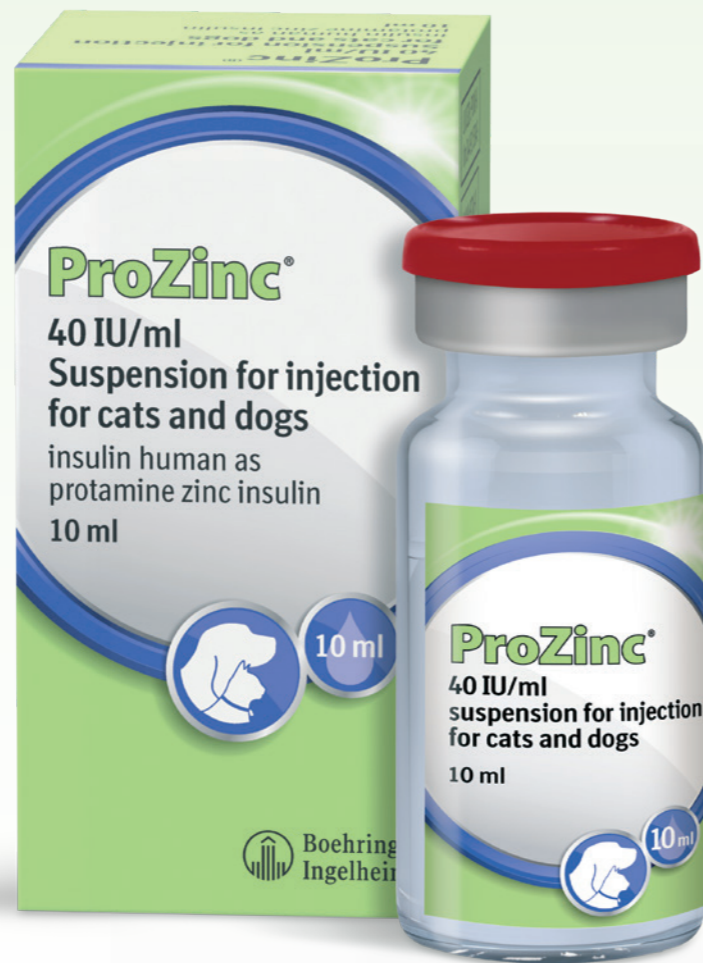
The aim is to maintain blood glucose below the renal threshold, but comfortably above levels that risk hypoglycaemia. This is achieved when glucose levels are kept within the target range of 4.5- 14.0 mmol/l for as much of the day as possible, **requiring an insulin which lasts ideally around 12 hours for twice daily dosing, and 24 hours for once daily dosing**.



# PROZINC®: A LONGER-ACTING INSULIN<sup>1</sup>

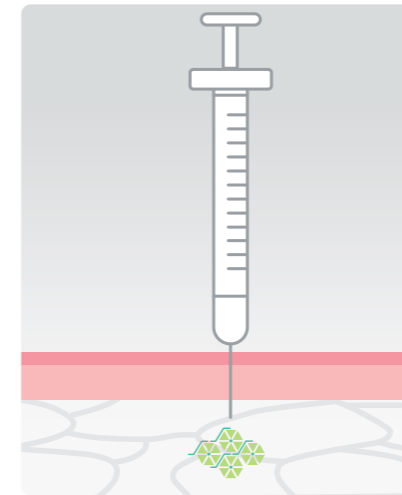
- Protamine Zinc Insulin (PZI)
- Licensed for **cats & now dogs**
- **Slow onset with a prolonged duration of action**
- Optimised for **twice daily use in cats** and **once daily use in dogs**<sup>2-8</sup>

- 40 IU/ml
- 10 ml bottle
- 60 day in-use shelf life
- U-40 ProZinc® syringes available

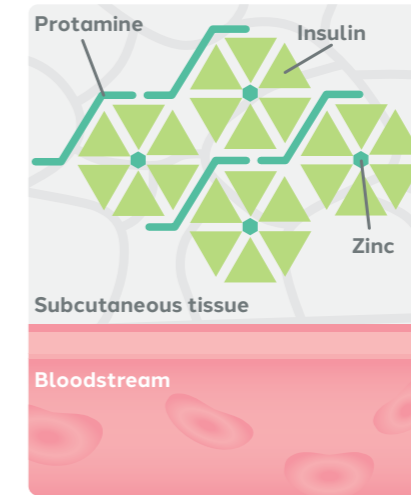


## ProZinc® is slowly released into the blood

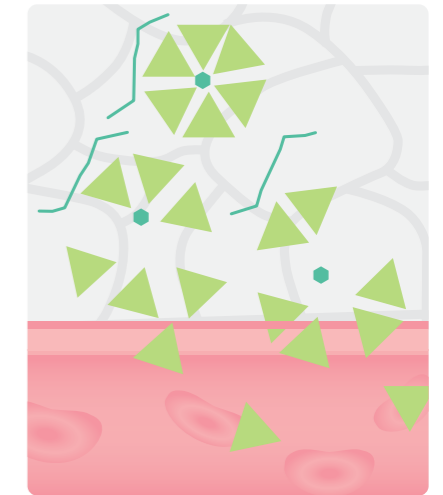
Protamine and zinc **slow the absorption of insulin** from the ProZinc® subcutaneous depot.<sup>1</sup>



Insulin, protamine and zinc form a depot under the skin following subcutaneous injection.



Insulin hexamers form around zinc which are stabilised by protamine.



The protamine-zinc-insulin depot is slowly degraded to gradually release active insulin monomers into the blood.

## ProZinc® is stable

ProZinc® **uses recombinant DNA technology**, which does not rely on an animal insulin source. This results in a high-quality insulin with a consistent duration of action. ProZinc® 10 ml has a **3 year shelf life from manufacture**, with an **unsurpassed 60 day in-use shelf life** after opening the vial – over 100% longer than other veterinary-licensed insulins.\*†

## With ProZinc® accurate administration is easy

ProZinc® is a 40 IU/ml insulin, enabling accurate dose titration, especially when combined with ProZinc® 0.3 ml syringes in cats and ProZinc® 1ml syringes in dogs (with 0.5 IU and 1 IU graduations respectively).



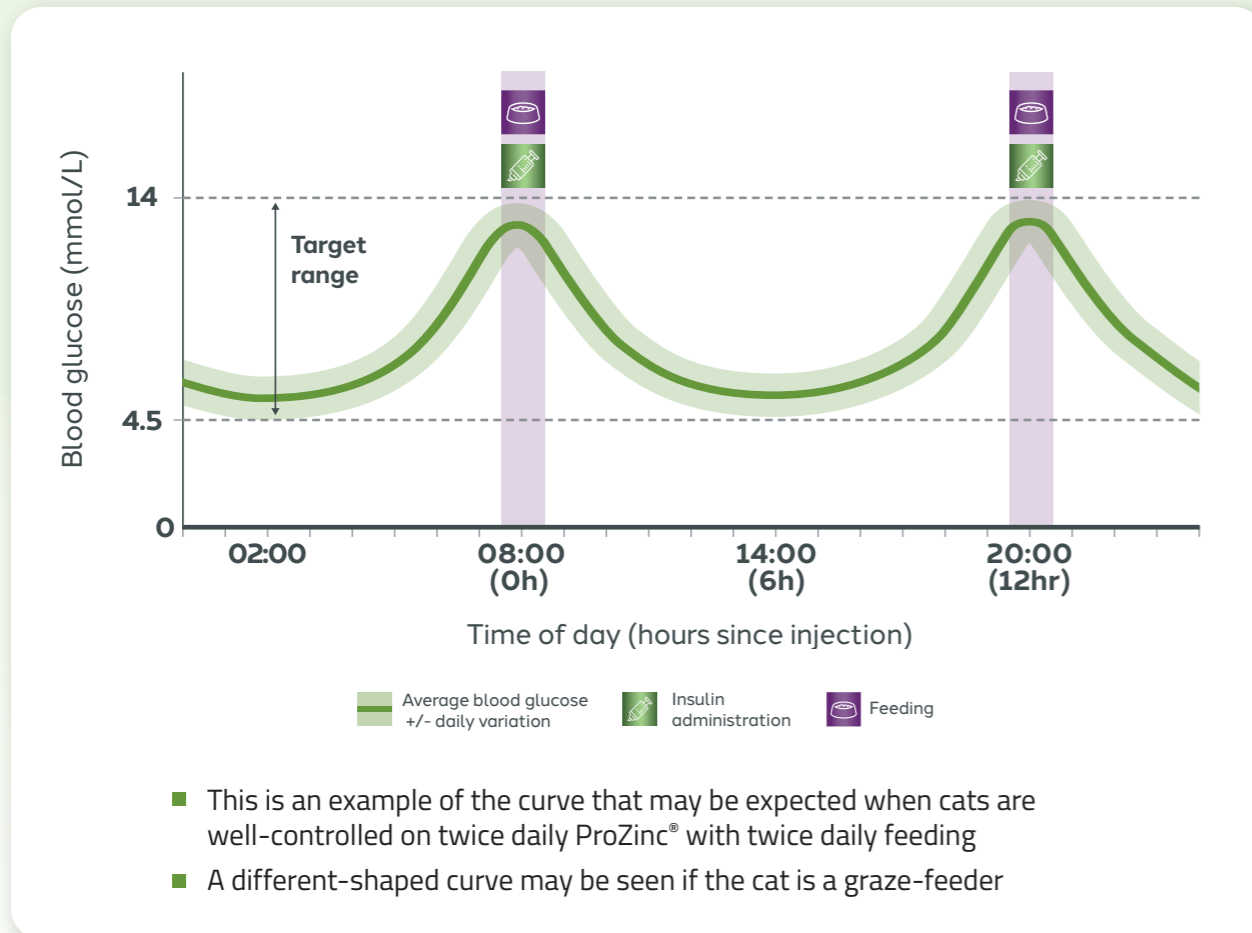
\*Both unopened and opened ProZinc® bottles should be stored upright in a refrigerator (2°C-8°C) but should not be frozen. ProZinc® should be mixed by gently rolling the bottle prior to withdrawing the dose.

†Caninsulin® shelf life – as packaged for sale: 2 years; after first opening of immediate packaging: 28 days (Summary of Product Characteristics).

# PROZINC® IN CATS

## Optimised for twice daily dosing

ProZinc® has a **duration of action of 11.5-18.5 hours in cats**.<sup>2</sup> This makes ProZinc® suited to twice daily dosing in cats, giving a shallow glucose curve with the next dose given before the previous dose runs out. A 'wrap around' action can therefore be achieved, limiting periods of hyperglycaemia above the target range.



## Recommended by experts

There are two international, peer-reviewed guidelines that help guide veterinary treatment of diabetes in cats:

- ISFM Consensus Guidelines on the Practical Management of Diabetes Mellitus in Cats (2015)<sup>3</sup>
- AAHA Diabetes Management Guidelines for Dogs and Cats (2018)<sup>4</sup>

Both of these guidelines recommend the use of longer-acting insulins such as PZI for treatment and management of diabetes in cats.

*"The use of longer-acting insulin preparations, injected twice daily, is recommended for optimal diabetic control"<sup>3</sup>*



*"In the UK, the only veterinary licensed longer acting insulin preparation is a protamine zinc insulin (ProZinc®) and this is an appropriate choice for first-line use in uncomplicated diabetic cats"<sup>5</sup>*



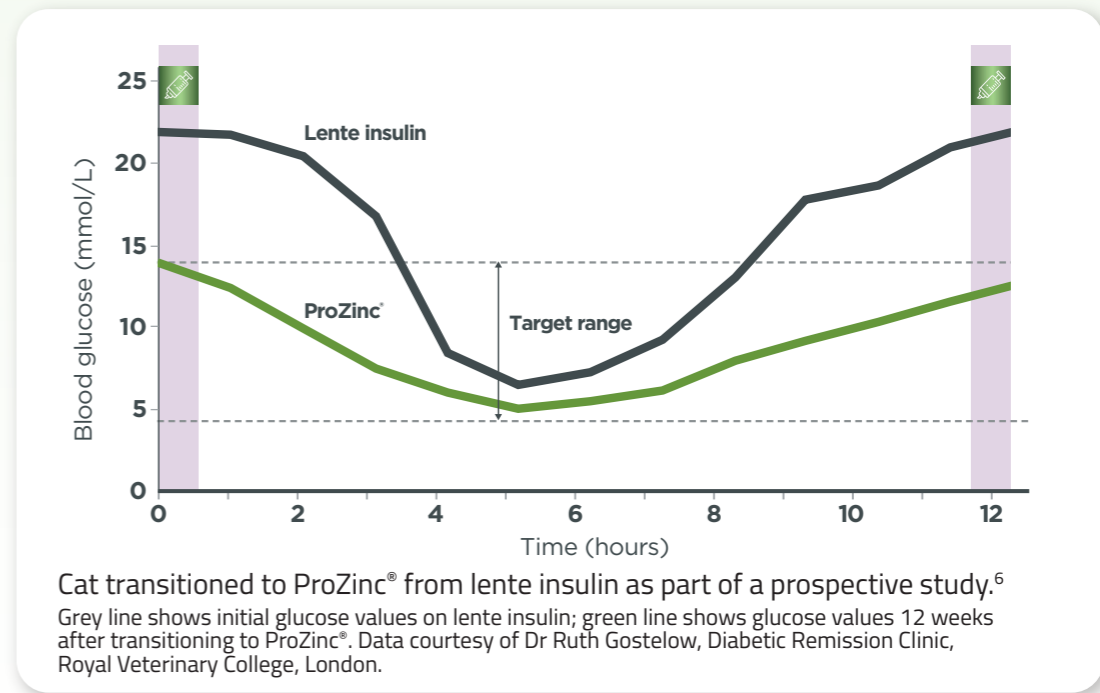
**Dr Martha Cannon**  
BA VetMB DSAM(Fel) FRCVS  
RCVS Specialist in Feline Medicine

## Improved control compared to lente insulin<sup>6</sup>

Cats that were transitioned from lente insulin to ProZinc® at the Royal Veterinary College's Diabetic Remission Clinic demonstrated significant improvement in:<sup>6</sup>

- Clinical signs
- Quality of life
- Fructosamine

All cats with short duration of action on lente insulin showed longer duration of action on ProZinc®.

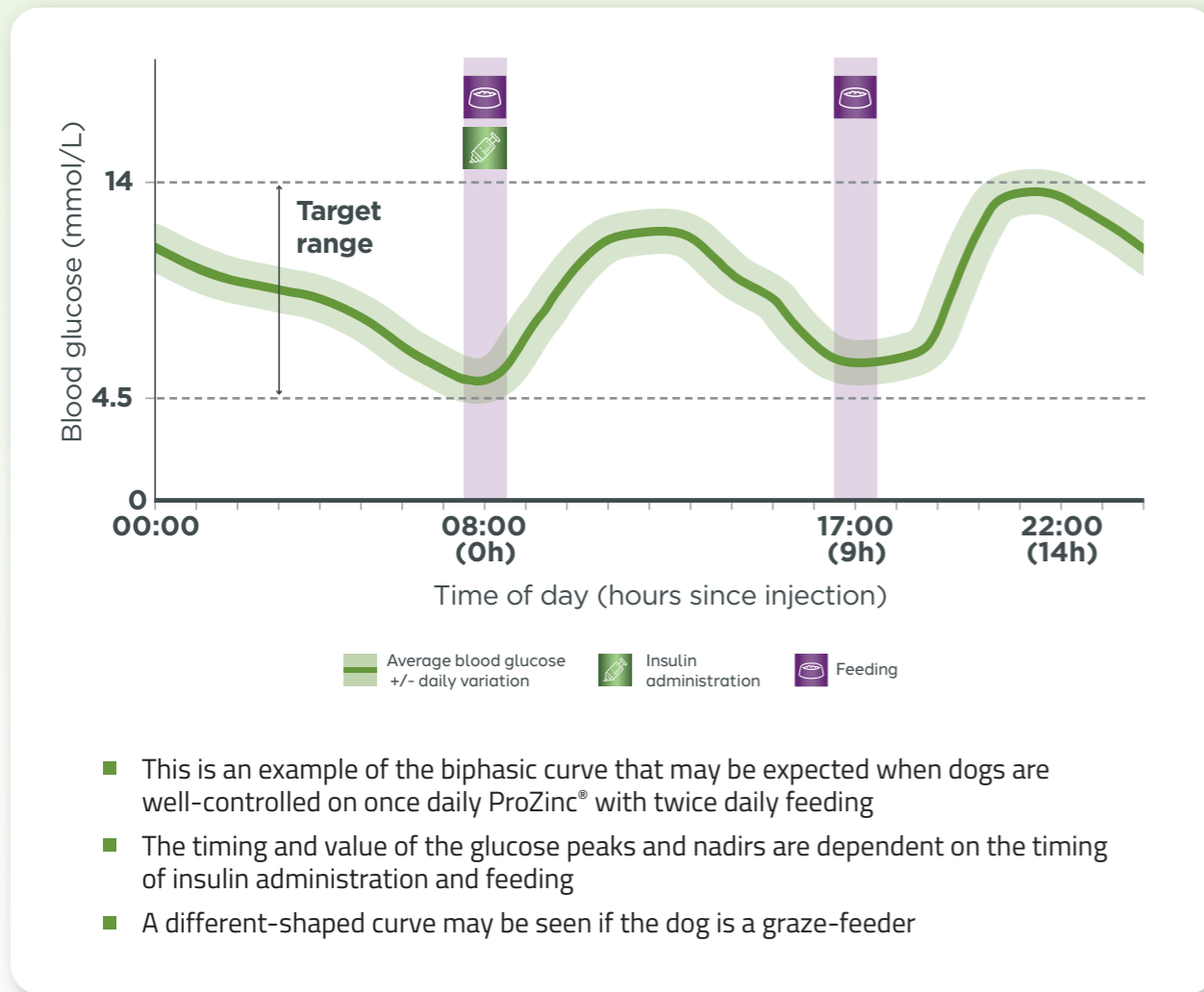


# PROZINC® IN DOGS

## Duration of action in dogs can make once daily control achievable

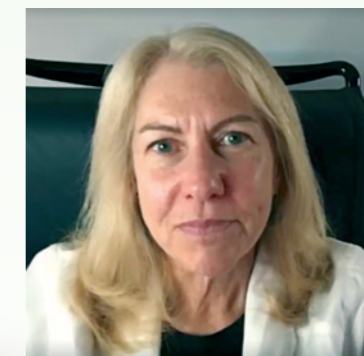
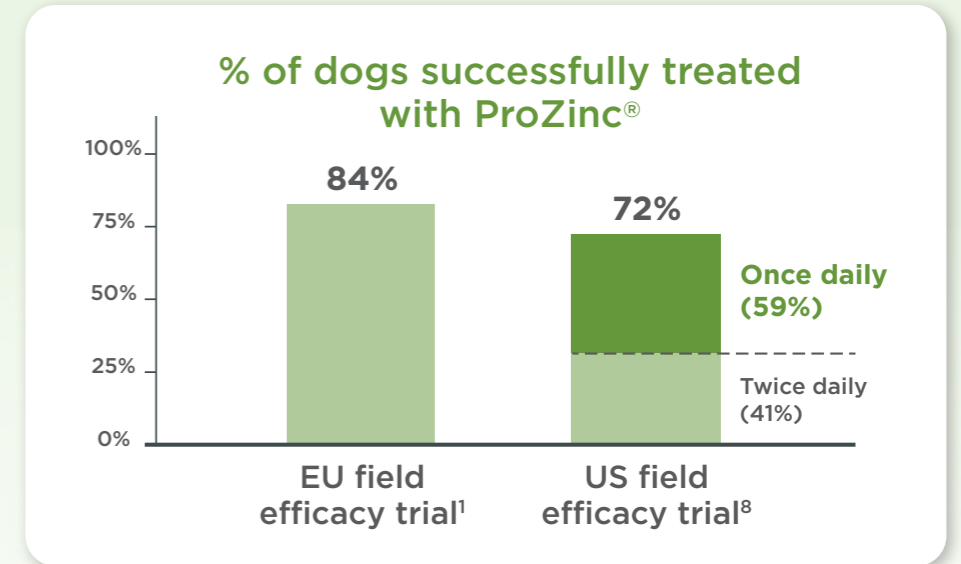
Dogs metabolise insulin more slowly than cats, and ProZinc® is no exception, having a **duration of action of around 20-22 hours in dogs<sup>7</sup>**, which can make once daily control a reality. The aim of once daily ProZinc® in dogs is to provide a 'background' level of insulin to control glucose levels following feeding.

It is important to be aware this can sometimes result in unexpected glucose curves: **it is not unusual for dogs controlled with once daily ProZinc® to have glucose levels within the lower half of the target range at the time of ProZinc® injection<sup>7</sup>**. This is why it is especially important in dogs to focus on clinical control and not solely on blood glucose curves (also refer to the diabetes management flowchart on page 16). For those dogs which metabolise ProZinc® more quickly, twice daily control will usually present more like a 'classic' glucose curve.



## Clinical efficacy has been demonstrated in diabetic dogs in the real world

- **European field efficacy trial:<sup>1</sup>**
  - Dogs randomly treated with lente or ProZinc® insulin **over 12 weeks**
  - **84%** overall treatment success with ProZinc®
- **US clinical efficacy trial:<sup>8</sup>**
  - Largest ever canine diabetes trial with **276 dogs receiving ProZinc® over 12 weeks**
  - **72%** overall treatment success with ProZinc®
  - Most dogs (**59%**) successfully treated with ProZinc® received it just **once daily**



**Dr Cynthia Ward**  
DVM PhD DipACVIM SAIM  
Director of the Veterinary Diabetes Clinic  
University of Georgia

*"The high percentage of once daily treated dogs showing improvement in diabetic parameters & clinical signs confirms the long duration of action of PZI, which will positively impact the lives of both diabetic dogs & their owners"<sup>8</sup>*

Give your canine patients the chance of once daily control with ProZinc®

# HOW TO SUCCESSFULLY USE PROZINC®

## 1. Make a confident diagnosis, then start ProZinc®

### Diagnosis of diabetes mellitus is based on:

- **Clinical signs**
  - Polyuria (PU), polydipsia (PD), polyphagia and weight loss
  - If the patient is anorexic, test for diabetic ketoacidosis (DKA) and manage accordingly
- **Supporting laboratory results**
  - Hyperglycaemia with glucosuria on at least two occasions
  - Fructosamine is recommended in cats to differentiate between stress hyperglycaemia and diabetes (and can also support a diagnosis in dogs), as well as serving as a baseline measurement

### Additional data to help detect concurrent disease includes:

- Haematology and biochemistry (including T4 in cats)
- Full urinalysis, including culture
- Blood pressure

### Start ProZinc® alongside an appropriate supporting regime



#### CATS

Start 0.2-0.4 IU/kg ProZinc® twice daily\*  
(12 hours apart)  
Round total dose down to nearest 0.5 IU

#### Feeding

- Either twice daily at the time of injection or grazing throughout the day
- A low carbohydrate diet has been shown to improve control<sup>3</sup>



#### DOGS

Start 0.5-1.0 IU/kg ProZinc® once daily†  
(around the same time every morning)  
Round total dose down to nearest 0.5-1 IU

#### Feeding

- Twice daily, at the time of injection & then 8-10 hours later
- A higher fibre diet may help to slow postprandial glucose release<sup>4</sup>

### Minimise potential causes of insulin resistance:

- Optimise bodyweight, neuter females & stop diabetogenic medications if possible
- Control concurrent endocrine and inflammatory conditions (e.g. hyperadrenocorticism, hyperthyroidism, dental disease, UTIs)

### Exercise dogs at least once daily (ideally at a similar time)

- This can improve sensitivity to insulin

### Form a partnership with the owner

- Show owners how to inject
- Teach owners about diabetes & when to seek help
- Use ProZinc® booklets, ProZinc® Home Care Journals & injection videos
- Inform owners it can take a couple of months to achieve control



## 2. Monitor the patient

### Good control should primarily be based on improved clinical signs:

- Reduction in PU/PD and polyphagia, optimisation of weight and muscle mass, no signs of hypoglycaemia or diabetes progression
- Owners can use the ProZinc® Home Care Journal to keep a record for review

### Allow time for ProZinc® to work after initiating treatment and after dose changes:

- Reassess every 1-2 weeks until control is achieved, then reassess 1 month later
- Subsequent ongoing assessments should ideally happen every 3-4 months

### Glycaemic testing

- **Blood glucose curves**
  - Full blood glucose curves are generally not required whilst stabilizing patients with ProZinc®
  - A few blood glucose readings can be used to help identify the lowest glucose value (nadir): around 6-9 hours after injection in cats, & 8-10 hours in dog<sup>2,7</sup>
  - Glucose testing can be performed in the clinic, or at home with appropriate owners
  - A more extensive (e.g. 10-14 hour) blood glucose curve can sometimes be helpful to further investigate insulin duration of action or suboptimal dosage
- **Fructosamine**
  - Reflects the blood glucose levels over the previous 2-3 weeks, so should not be used less frequently than this or if the ProZinc® dose was changed within this timeframe
  - Useful to help build up the picture of overall control
- **Urine glucose & ketones**
  - Urine dipsticks can be used by owners to check for presence of glucose, and absence of ketones
  - Small amounts of glucose are expected, whilst continued absence can indicate periods of hypoglycaemia, or impending remission in cats
  - The owner should contact their vet practice if ketones are present or glucose is absent
- **Interstitial glucose monitoring**
  - An increasingly popular method of monitoring glycaemic control
  - Devices such as the FreeStyle Libre® gather several days of glucose data at home without the need for repeated blood glucose testing
  - These results can be reviewed remotely, decreasing the stress with hospital glucose curves
  - For more information please contact our Technical Services team (contact details on page 17 and the back cover)

Evaluation of control in diabetic cats and dogs should be based primarily on clinical signs

And remember the golden rule: 'Be patient with your patient!'

# HOW TO SUCCESSFULLY USE PROZINC®

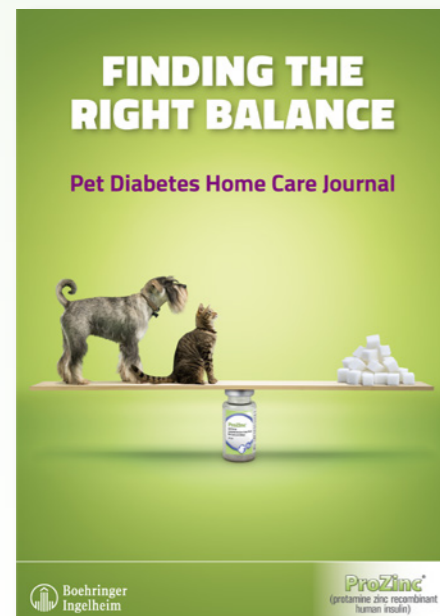
## 3. Reassess regularly

### First reassessment

- Timing can be based on owner confidence with injections
  - Usually 1-2 weeks but earlier if owner requires additional support
- Ask the owner to demonstrate drawing up insulin and the injection procedure
  - Sterile water for injection or saline can be helpful for this
- Weigh the patient and assess muscle mass
- Review the ProZinc® Home Care Journal to help assess clinical control
  - Consider signs of hyper- and hypoglycaemia
- Dose adjustments are usually not necessary at the first revisit - **be patient with your patient!**

### Ongoing reassessments until stable

- Continue reassessments and dose titration based on clinical signs every 1-2 weeks
  - Until there is good control
  - Refer to dose adjustment section on page 14
- Weigh the patient and assess muscle mass
- Review the ProZinc® Home Care Journal to help assess clinical control
  - Consider signs of hyper- and hypoglycaemia
- Check for any compliance issues



The ProZinc® Home Care Journal helps pet owners to assess improvement or worsening of clinical signs and changes in routine



### Reassessment 1 month after becoming stable

- Weigh the patient and assess muscle mass
- Review the ProZinc® Home Care Journal to help assess clinical control
  - Consider signs of hyper- and hypoglycaemia
- Consider checking serum fructosamine
- If control has been lost:
  - Rule out compliance problems, poor handling/storage of ProZinc®, activity or diet change
  - Check for concurrent diseases which could be causing insulin resistance (e.g. hyperadrenocorticism, hyperthyroidism, inflammatory conditions such as dental disease & UTIs)
  - Consider a 10-14 hour blood glucose curve or intersitital glucose monitoring (e.g. with Freestyle Libre®) to rule out short duration of action of insulin, Somogyi phenomenon and suboptimal dosing
- No clinical signs: reassess in 3-4 months

### Ongoing reassessments of the stabilised patient

- Ideally every 3-4 months
- Weigh the patient and assess muscle mass
- Review the ProZinc® Home Care Journal to help assess clinical control
  - Consider signs of hyper- and hypoglycaemia
- Consider checking serum fructosamine

A patient is considered stable when their clinical signs, bodyweight & condition are under control, fructosamine (if measured) is under 450 µmol/l, and there is no evidence of hypoglycaemia or other diabetes-related complications (e.g. ketosis, ketoacidosis, cataracts)



# HOW TO SUCCESSFULLY USE PROZINC®

## 4. Adjust the ProZinc® dose gradually for optimal control

### General principles

- A decision to increase dose should mainly be based on continued presence of clinical signs
  - Whilst the decision can be supported by glycaemic measures such as glucose curves, be cautious about interpreting these in isolation
- As ProZinc® has a prolonged duration of action, dose changes take a while to take effect
  - ProZinc® dose should not be increased more frequently than every 1-2 weeks
- It may take at least 4-6 weeks to gain good control, so be patient with your patient!
  - Do not be tempted to increase the dose too quickly

### Adjusting the dose

- If the patient is not yet controlled, increase the ProZinc® dose (also refer to management flowchart on page 16):



#### CATS

Increase ProZinc® by  
0.5-1.0 IU per dose\*



#### DOGS

Increase ProZinc® by  
up to 25% per dose

### What if the patient is still difficult to control after 4-6 weeks?

- If clinical signs persist:
  - Rule out compliance problems, poor handling/ storage of ProZinc®, change in activity or diet
  - Perform a 10-14 hour blood glucose curve or interstitial glucose monitoring (e.g. FreeStyle Libre®) to investigate insulin duration of action or suboptimal dosage
- Adjust the ProZinc® regime following the results from glucose monitoring:
  - **Short duration of action in dogs** (blood glucose rising above 14 mmol/l within 14 hours after ProZinc® injection with no subsequent decrease prior to next ProZinc® injection):
    - **Switch to twice daily dosing**
      - Reduce the once daily ProZinc® dose by one third and give this reduced dose twice daily
      - Feed and give ProZinc® around the same time approximately 12 hours apart
  - **Hypoglycaemia** (glucose <4.5 mmol/l along with clinical signs such as lethargy, weakness, ataxia, seizures; or glucose <3.5 mmol/l without clinical signs), or **Somogyi phenomenon**†:
    - **Reduce or restart ProZinc®**
      - Reduce ProZinc® by 25-50% per dose, or:
      - Restart at 0.2-0.4 IU/kg per dose (cats) or 0.5 IU/kg per dose (dogs)
  - **Normal glucose & fructosamine in cats** (especially with ProZinc® < 1.0 IU per dose) can indicate **diabetic remission**:
    - **Reduce or withdraw ProZinc®**
      - Reduce ProZinc® by 0.25-1.0 IU per dose every 1-2 weeks
      - If glucose measurements are in the low or low-normal range then stop ProZinc®
      - Recheck blood glucose in one month or earlier if clinical signs return

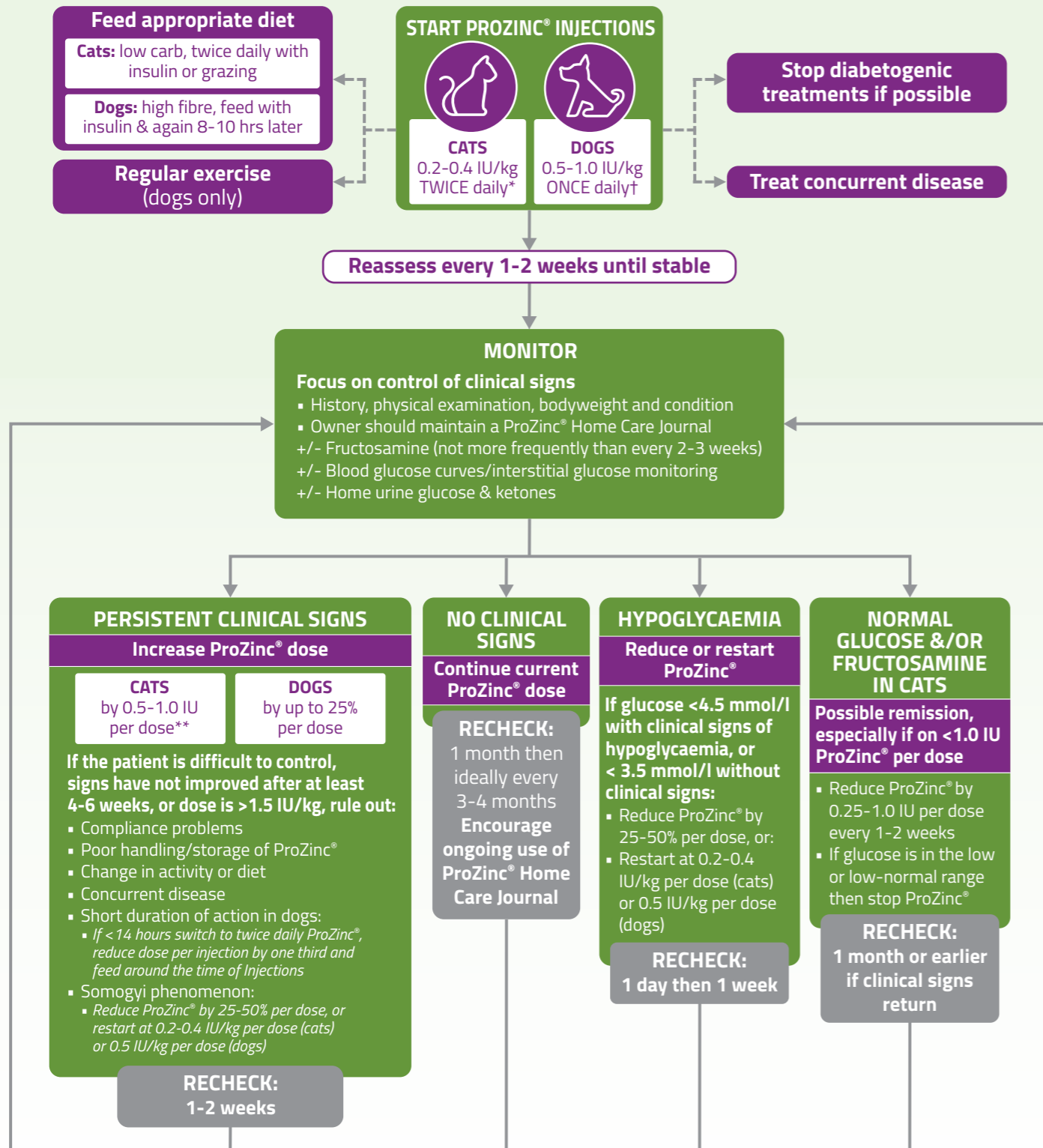


†The Somogyi, or "overswing" phenomenon (also referred to as hypoglycaemia-induced hyperglycaemia) refers to hypoglycaemia followed by marked hyperglycaemia. It usually results from rapid escalation in insulin dose, and the resultant hyperglycaemia can last for a long time – a day or more – which can be confused with inadequate insulin dose, when in fact the dose is too high.



# PROZINC® STABILISATION FLOWCHART

Evaluation of control with ProZinc® should be based primarily on clinical signs, with glucose monitoring helping to support decisions as required.



\*For cats previously controlled on insulin, a higher starting dose up to 0.7 IU/kg may be appropriate. \*\*If nadir is unknown or nadir < 8 mmol/l choose 0.5 IU/dose, if nadir > 8 mmol/l choose 1.0 IU/dose. †For newly diagnosed diabetic dogs, a starting dose of 0.5 IU/kg once daily is recommended

# OWNER AND VETERINARY SUPPORT

## Pet owner support

### ProZinc® pet owner guides

Provide educational and empowering information on diabetes and its management for owners of pets that have been prescribed ProZinc®.

### ProZinc® home care journal

Provides owners a convenient place to record important information about their pet's health and treatment for review at reassessments. Helps keep focus on the clinical picture.

All available for owners on [www.prozinc.co.uk](http://www.prozinc.co.uk).

### ProZinc® administration videos

Demonstrations of preparing and administering ProZinc®, along with educational tips to ensure owners are comfortable with injecting.



## Veterinary support

### Diabetes management tools

Diabetes management guides, flowcharts and also glucose curve templates are available to help you best manage diabetes with ProZinc®. Available from your Boehringer Ingelheim territory manager.



### Technical services helpline

Recently awarded 'Best in Class' animal health pharmaceutical company technical helpline,<sup>9</sup> our Technical Services team comprises 7 vets with over 75 years total experience in small animal practice. They are there to help you manage diabetes in cats and dogs with ProZinc® – just call 01344 746957 (UK) or 01 291 3985 (IE), or email [vetenquiries@boehringer-ingelheim.com](mailto:vetenquiries@boehringer-ingelheim.com). There is also a 24/7 365 emergency advice service.



ProZinc® information and diabetes CPD delivered by key experts in the form of short videos, webinars and articles – it's free and counts towards your annual CPD! Visit [www.boehringer-academy.co.uk](http://www.boehringer-academy.co.uk) now.

### Virtual vet support

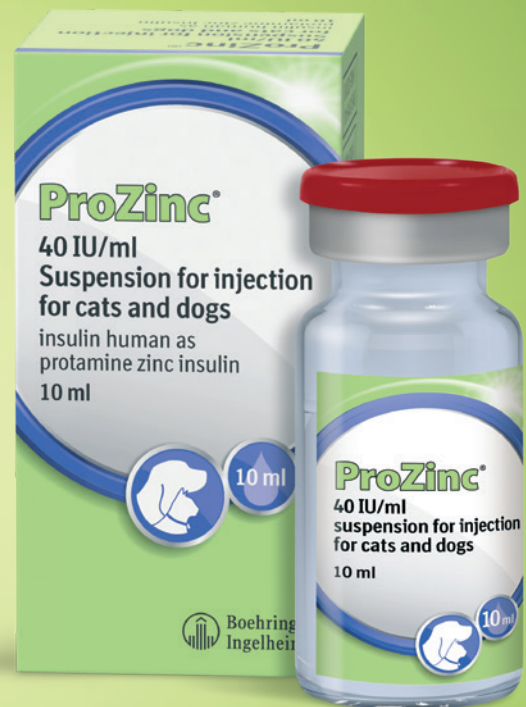
Would you like to discuss technical aspects of using ProZinc® to manage diabetes in cats and dogs during a practice meeting?

Why not get one of our technical vets to join over Microsoft Teams or Zoom – just ask your territory manager to arrange a session. We can even provide (a real) lunch!



# MAKE PROZINC® YOUR FIRST-CHOICE INSULIN

- Prolonged duration of action
- Optimised for twice daily dosing in cats
- Offers once daily convenience for dog owners



- For general ProZinc® sales enquiries contact your local Boehringer Ingelheim Animal Health territory manager or phone 01344 746959 (UK) or 01 291 3985 (IE).
- For ProZinc® technical enquiries contact technical services on [vetenquiries@boehringer-ingelheim.com](mailto:vetenquiries@boehringer-ingelheim.com) or phone 01344 746957 (UK) or 01 291 3985 (IE).

**References:** 1. European Public Assessment Report (EPAR): ProZinc® (protamine zinc recombinant human insulin). London: European Medicines Agency. Available at [www.ema.europa.eu](http://www.ema.europa.eu). 2. Ward, C.R. (2015) Efficacy of ProZinc® insulin in naive and insulin-established cats using continuous interstitial glucose monitoring. *J Vet Intern Med* 29, 1171–1172. 3. Sparkes, A.H. et al. (2015) ISFM Consensus Guidelines on the Practical Management of Diabetes Mellitus in Cats. *J Feline Med Surg* 17, 235–50. 4. Behrend, E. et al. (2018) 2018 AAHA Diabetes Management Guidelines for Dogs and Cats. *J Am Anim Hosp Assoc* 54, 1–21. 5. Cannon, M. (2018) Diabetes mellitus in cats. *In Practice* 40, 170–179. 6. Gostelow, R. et al. (2018) Prospective evaluation of a protocol for transitioning porcine lente insulin-treated diabetic cats to human recombinant protamine zinc insulin. *Journal of Feline Medicine and Surgery* 20, 114–121. 7. Ward, C.R. et al. (2021) Assessment of once daily dosing with ProZinc® insulin in diabetic beagle dogs. *Journal of Veterinary Internal Medicine* 35, 3030. 8. Ward, C.R. et al. (2021) Field efficacy and safety of protamine zinc recombinant human insulin in 276 dogs with diabetes mellitus. *Domestic Animal Endocrinology* 75, 106575. 9. CMresearch (2022) Small animal vets UK April 2022. Syndicated Sales Rep Survey.

ProZinc® contains protamine zinc recombinant human insulin. ProZinc® is indicated for the treatment of diabetes mellitus in cats and dogs to achieve reduction of hyperglycaemia and improvement of associated clinical signs. UK: POM-V IE: POM. For information about side effects, precautions, warnings and contraindications please refer to the product packaging and package leaflet. Further information available in the SPC or from Boehringer Ingelheim Animal Health UK Ltd., RG12 8YS, UK. UK Tel: 01344 746959 (sales) or 01344 746957 (technical), IE Tel: 01 291 3985 (all queries). Email: [vetenquiries@boehringer-ingelheim.com](mailto:vetenquiries@boehringer-ingelheim.com). ProZinc® is a registered trademark of Boehringer Ingelheim Vetmedica GmbH, used under licence. ©2022 Boehringer Ingelheim Animal Health UK Ltd. All rights reserved. Date of preparation: December 2022. UI-PVT-0094-2022. Use Medicines Responsibly.



**ProZinc®**  
(protamine zinc recombinant human insulin)