SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ProZinc 40 IU/ml suspension for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Insulin human*……40 IU as protamine zinc insulin.

One IU (International Unit) as protamine zinc insulin equivalent to 0.0347 mg of insulin human.

*produced by recombinant DNA technology.

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Protamine sulfate	0.466 mg
Zinc oxide	0.088 mg
Phenol	2.5 mg
Glycerol	
Dibasic sodium phosphate, heptahydrate	
Hydrochloric acid (for pH adjustment)	
Sodium hydroxide (for pH adjustment)	
Water for injections	

Cloudy, white, aqueous suspension.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use, specifying the target species

For the treatment of diabetes mellitus in dogs to achieve reduction of hyperglycaemia and improvement of associated clinical signs.

3.3 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.

3.4 Special warnings

Very stressful events, inappetence, concomitant treatment with gestagens and corticosteroids or other concomitant diseases (e.g. gastro-intestinal, infectious or inflammatory or endocrine diseases), might influence insulin effectiveness and therefore the insulin dose may need to be adjusted.

3.5 Special precautions for use

Special precautions for safe use in the target species:
The insulin dose may need to be adjusted or discontinued after resolution of transient diabetic stages (e.g. dioestrus-induced diabetes mellitus, diabetes mellitus secondary to hyperadrenocorticism).

After the daily insulin dose is established, monitoring for diabetic control is recommended.
Treatment with insulin can cause hypoglycaemia, for clinical signs and appropriate treatment, see section 3.10.

In cases where hypoglycaemia is suspected, blood glucose measurements should be taken at the time of occurrence (if possible) as well as shortly prior to the next feeding/injection (where applicable).
Stress and irregular exercise should be avoided. It is recommended to establish a regular twice daily feeding schedule with the owner whether injecting insulin once or twice daily.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Accidental self-injection can provoke clinical signs of hypoglycaemia which may be treated by oral administration of sugar. There is a low possibility of an allergic reaction in sensitised individuals.

In case of accidental self-injection seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Very common (> 1 animal in 10 animals treated):	Hypoglycaemia (increased appetite, anxiety, twitching, stumbling gait[1], disorientation)[2].
Very rare (< 1 animal in 10,000 animals treated, including isolated reports).	Injection site reactions[3].

[1] Unstable locomotion and sinking in the rear legs.
[2] Generally mild in nature. Immediate administration of a glucose containing solution or gel and/or food is required. Insulin administration should be temporarily stopped, and the next dose of insulin adjusted appropriately.
[3] Resolved without cessation of therapy.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during breeding, pregnancy and lactation.
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.

3.8 Interaction with other medicinal products and other forms of interaction

Changes in insulin requirements may result from administration of substances which alter glucose tolerance (e.g. corticosteroids and gestagens). Monitoring of glucose concentrations should be performed to adjust the dose accordingly. Similarly, changing the diet may alter insulin requirements and necessitate a change of insulin dose.

3.9 Administration route and dosage

Subcutaneous use.

If the animal owner is to administer the veterinary medicinal product, suitable training/advice should be provided by the prescribing veterinarian before using for the first time.

Dosage:
The veterinarian should re-evaluate the animal at appropriate intervals and make adjustments to the treatment protocol, for instance dose and dosing regimen, until adequate glycaemic control has been attained.

Any dose adjustment (i.e. increase of dose) should be in general performed after several days (e.g. 1 week) since full action of insulin requires an equilibration phase. Dose reductions due to observed hypoglycaemia or suspected Somogyi effect (rebound hyperglycaemia) may be of 50% or higher (potentially including a temporary pause of insulin administration).

Once adequate glycaemic control is achieved intermittent glucose monitoring should be performed, especially when there is a change in clinical signs, and further adjustments in the insulin dose might be necessary.

General guidance:
Dosing should be individualised and based on the clinical presentation of each patient.

To achieve optimal control of diabetes mellitus, dose adjustments should primarily be based on clinical signs. Blood parameters such as fructosamine, maximum blood glucose and decrease of blood glucose concentrations in blood glucose curves conducted over a sufficient period of time to determine a blood glucose nadir should be used as supporting tools.
Re-evaluation of clinical signs and laboratory parameters should be performed as recommended by the attending veterinarian.

Initiation:
For initiation of treatment, the recommended dose is 0.5 to 1 IU insulin/kg bodyweight once daily every morning (approx. every 24 hours).
For newly diagnosed diabetic dogs, a starting dose of 0.5 IU insulin/kg once daily is recommended.

Management:
Adjustments of insulin dose on a once daily regimen, if required, should generally be done in a conservative and gradual manner, (e.g. up to 25% increase/decrease of the dose per injection).

If insufficient improvement in diabetic control is observed after an adequate dose adjustment period of 4 to 6 weeks on once daily treatment, the following options may be considered:
- Further adjustments of insulin dose on once daily treatment may be necessary; in particular if dogs undertake increased physical activity, have a change of their usual diet or during concomitant illness.
- Switching to twice daily dosing: In such cases, it is recommended to reduce the dose per injection by one third (e.g. 12 kg dog being treated once daily with 12 IU insulin/injection may be switched to 8 IU insulin/injection administered twice daily). The veterinary medicinal product should be administered in the morning and in the evening, approx. 12 hours apart. Further adjustments of insulin dose on twice daily treatment may be necessary.

Depending on the underlying cause (e.g. dioestrus-induced diabetes mellitus), dogs can develop diabetic remission, although seldom. In those cases, sufficient endogenous insulin production will be regained and the exogenous insulin dose will need to be adjusted or ceased.

Method of administration:
A U-40 syringe must be used.
The suspension should be mixed by gently rolling the vial prior to withdrawing each dose from the vial.
The dose should be given concurrently with or immediately after a meal.
Particular care should be taken with regard to the accuracy of dosing.
The veterinary medicinal product should be administered by subcutaneous injection.
Avoid introduction of contamination during use.
After gently rolling the vial, veterinary medicinal product suspension has a white, cloudy appearance.
A white ring may be seen in the neck of some vials, but this does not affect the quality of the veterinary medicinal product.
Agglomerates (e.g. clumps) can form in insulin suspensions: do not use the veterinary medicinal product if visible agglomerates persist after gently rolling the vial.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

An overdose of insulin can result in hypoglycaemia in which case immediate administration of a

glucose containing solution or gel and/or food is required.

Clinical signs may include hunger, increasing anxiety, unstable locomotion, muscle twitching, stumbling or sinking in the rear legs and disorientation.
Insulin administration should be temporarily stopped and the next dose of insulin adjusted appropriately.
The owner is advised to have glucose containing products (e.g. honey, dextrose gel) in the household.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QA10AC01.

4.2 Pharmacodynamics

Insulin activates insulin receptors and therewith a complex cell signalling cascade which results in increased glucose uptake into the cells. The main effects of insulin are the reduction in circulating blood glucose concentrations and the storage of fat. Overall insulin influences the regulation of the carbohydrate and fat metabolism.

In an experimental study in healthy dogs, the time to blood glucose nadir after a single subcutaneous injection of 0.8 or 0.5 IU/kg bodyweight of the veterinary medicinal product was variable between dogs (range 3 to >24 hours), as was the duration of insulin action (range 12 to >24 hours). Median time to blood glucose nadir was approximately 16 and 12 hours following administration of 0.5 or 0.8 IU/kg bodyweight, respectively.

Under clinical field conditions in diabetic dogs, time to maximal effect in lowering blood glucose concentrations (i.e. blood glucose nadir) after subcutaneous administration was not observed within 9 hours after last injection in 67.9% of dogs overall. (73.5% on once daily and 59.3% on twice daily administration). Consequently, blood glucose curves should be conducted over a sufficient period to determine a blood glucose nadir.

4.3 Pharmacokinetics

<u>Absorption:</u>
Protamine zinc recombinant human insulin is an insulin whose absorption and onset of action is delayed by the addition of protamine and zinc leading to crystal formation. After subcutaneous injection, proteolytic tissue enzymes degrade protamine to permit the absorption of insulin. In addition, interstitial fluid will dilute and break down the formed zinc insulin hexamer complexes and result in a delayed absorption from the subcutaneous depot.

Distribution:
Once absorbed from the subcutaneous site, insulin will enter the circulation and diffuse into tissues, where it binds to insulin receptors found on most tissues. Target tissue organs are i.e. liver, muscle and adipose tissue.

Biotransformation:
Following the binding of insulin with the insulin receptor and the subsequent action, insulin is released back into the extracellular environment. It may then be degraded on passage through the liver or by the kidney. Degradation normally involves endocytosis of the insulin-receptor complex, followed by the action of insulin-degrading enzyme.

Elimination:
The liver and the kidney are the two main organs which eliminate insulin from the circulation. Forty per cent of insulin is eliminated by the liver and 60% is eliminated by the kidney.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 60 days.

5.3 Special precautions for storage

Store upright in a refrigerator (2 °C – 8 °C).
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

20 ml clear glass vial closed with a butyl rubber stopper and sealed with a plastic flip-off cap.

Package size: Cardboard box with one 20 ml vial.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica GmbH

7. MARKETING AUTHORISATION NUMBER

Vm 61700/5079

8. DATE OF FIRST AUTHORISATION

12 July 2013

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

May 2025

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Find more product information by searching for the 'Product Information Database' on www.gov.uk.

Gavin Hall
Approved: 18 August 2025