1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Caninsulin 40 IU/ml suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Insulin* 40 IU.
*Porcine insulin present as 35% amorphous Zinc insulin and 65% crystalline Zinc insulin.

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Zinc chloride	
Methyl parahydroxybenzoate (E218)	1.00 mg
Sodium acetate trihydrate	
Sodium chloride	
Hydrochloric acid (for pH adjustment)	
Sodium hydroxide (for pH adjustment)	
Water for injection	

A white to almost white suspension for injection.

3. CLINICAL INFORMATION

3.1 Target species

Dogs and cats.

3.2 Indications for use for each target species

For use in cases of diabetes mellitus (insulin deficiency) in dogs and cats, where the required blood glucose levels are achieved by using an individually adjusted dose of the veterinary medicinal product.

3.3 Contraindications

Do not administer intravenously.
Do not use in case of hypersensitivity to porcine insulin or to any of the excipients.

3.4 Special warnings

In cats, diabetic remission may be possible.

3.5 Special precautions for use

Special precautions for safe use in the target species:
It is important to establish a strict feeding schedule in consultation with the owner which will include a minimum of fluctuations and changes. See also information relating to owner precautions under "Maintenance" in section 3.9.
The use of progestogens (oestrus inhibitors) in patients suffering from diabetes mellitus should be avoided. Ovariohysterectomy may have to be considered.

Stress and irregular extra exercise must be avoided.
Care must be taken with the use of corticosteroids.
The veterinary medicinal product is a medium duration insulin and is not intended for the treatment of animals with severe acute diabetes presenting in a ketoacidotic state.

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 should be treated by oral administration of glucose.
In case of accidental self-injection seek medical advice immediately and show the package leaflet or label to the physician.

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

3.6 Adverse events

Dogs and cats:

Rare (1 to 10 animals / 10,000 animals treated):	Hypoglycaemia
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site reaction* Hypersensitivity reaction

*The reaction is usually mild and reversible.

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 the national competent authority via the national reporting system. See also the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
Use of the product during pregnancy or lactation requires close veterinary supervision to account for changes in metabolic requirements during this period.

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 such as corticosteroids, thiazide diuretics, progestagens and alpha-2 agonists. Monitoring of glucose levels should be used to adjust dose accordingly. Similarly, changes in diet or exercise routines may alter insulin requirements.

3.9 Administration routes and dosage

Owners should be instructed to have a box of powdered glucose at home before the product is administered. Administration of the product must be carried out by an adult responsible for the welfare of the animal.

Administer once or twice daily, as appropriate, by subcutaneous injection.
Alternate the injection site daily.

Invert the vial or cartridge before use until a homogenous, uniformly milky suspension is obtained. Foam on the surface of the suspension formed during shaking should be allowed to disperse before

the veterinary medicinal product is used and, if required, the veterinary medicinal product should be gently mixed to maintain a homogeneous, uniformly milky suspension before use. Agglomerates can form in insulin suspensions. Do not use the veterinary medicinal product if visible agglomerates persist after shaking thoroughly.
When using the veterinary medicinal product in vials:
A 40 IU/ml insulin syringe should be used.
When using the veterinary medicinal product in cartridges:
The cartridge is designed to be used with a re-usable pen injector (VetPen) available in two versions. VetPen 8 delivers 0.5 to 8 units of insulin per injection in 0.5 unit increments and VetPen 16 delivers 1 to 16 units of insulin per injection in 1.0 unit increments.
VetPens are accompanied by package leaflets with detailed instruction for use.

The duration of action may vary, making it necessary to administer an insulin dose twice daily to some diabetic dogs. In diabetic cats, it is necessary to administer the veterinary medicinal product twice daily. The dose depends on the degree of deficit in the animal's own insulin production and is therefore different in each case.

Stabilisation phase
Dogs: Insulin therapy is initiated with the starting dose of **0.5 to 1 IU/kg** bodyweight once daily, rounded down to the lowest entire number of units. To reduce the risk of hypoglycaemia, it is recommended to administer as low a dose as required within the starting dose range. Subsequent adjustment to establish the maintenance dose should be made by increasing or decreasing the daily dose by approximately 10% according to the evolution of the diabetes clinical signs and to the results of serial blood glucose measurement. Alterations in dose should not normally be made more frequently than every 3 to 7 days. Depending on the duration of insulin action, twice daily administration of insulin may be necessary. In a clinical study conducted using the product, the majority of diabetic dogs treated required twice daily administration in order to achieve adequate control. In such cases, the dose per injection must be decreased by 25% so that the total daily dose is less than doubled.
For example for a 10 kg dog receiving 5 IU once daily, the new dose (rounded down to the nearest whole unit) would be 3 IU per injection initially. The two daily doses should be administered at 12-hour intervals. Further dose adjustments should be made progressively as previously explained.
To achieve a balance between the generation of glucose and the effect of the veterinary medicinal product, feeding should be synchronised with the treatment and the daily ration divided into two meals. The composition and quantity of the daily food intake should be constant. In dogs treated once daily, the second meal is usually fed at the time of peak insulin effect.
In dogs treated twice daily, feeding should coincide with administration. Each meal should be fed at the same time each day.

Cats: The initial dose is **0.25 IU/kg or 0.5 IU/kg** per injection based on the baseline blood glucose concentration, as presented in the following table. Cats require twice daily administration.

Cat blood glucose concentration	**Starting dose per cat**
< 20 mmol/l or < 3.6 g/l (< 360 mg/dl)	0.25 IU/kg twice daily (up to a maximum of 2 IU per injection)
≥ 20 mmol/l or ≥ 3.6 g/l (≥ 360 mg/dl)	0.5 IU/kg twice daily (up to a maximum of 2 IU per injection)

The starting dose should not exceed 2 IU per injection.
The composition and quantity of the daily food intake should be constant.
Subsequent adjustment to establish the maintenance dose should be made by increasing or decreasing the daily dose according to the results of serial blood glucose measurement. Alterations in dose should not normally be made more frequently than every week. Increments of 1 IU per injection are recommended. Ideally, no more than 2 IU should be administered per injection in the first three weeks of treatment. Due to the day-to-day variation in the blood glucose response, and the variations in insulin responsiveness that are seen with time, larger or more frequent increases in dose are not recommended.

Maintenance phase in dogs and cats
Once the maintenance dose has been reached and the animal is stabilised, a long term management programme needs to be established. The aim should be to manage the animal in such a way as to minimise the variations in its insulin requirement. This includes clinical monitoring to detect under or overdosage of insulin and adjustment of dose if required. Careful stabilisation and monitoring will help to limit the chronic problems associated with diabetes, including cataracts (dogs), fatty liver (dogs and cats), etc.
Follow up examinations should be performed every 2-4 months (or more often if there are problems) to monitor the animal's health, the owners records, and urine glucose and biochemical parameters (like blood glucose and/or fructosamine concentration). Monitoring of urine glucose (if required) should be in accordance with and following the recommendations of the attending veterinarian. Adjustments to the insulin dose should be made based on interpretation of the clinical signs supported by the laboratory results.
Somogyi overswing, also called rebound hyperglycaemia, is a response to an overdose of insulin insufficient to cause, potentially fatal, hypoglycaemia. As hypoglycaemia begins to develop, a hormonal response is triggered which results in the release of glucose from hepatic glycogen stores. This results in rebound hyperglycaemia which may also manifest as glycosuria for part of the 24-hour cycle. There is a danger that the Somogyi overswing is interpreted as a requirement for increase in the insulin dose rather than a decrease. This can be avoided by basing decisions on serial blood glucose measurements rather than single point measurements. The ability of pet owners to recognise the signs of hypo- or hyperglycaemia and respond appropriately is very important.

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

Overdose of insulin results in clinical signs of hypoglycaemia. Signs of hunger, increasing anxiety, unstable locomotion, muscle twitching, stumbling or sinking in the rear legs and disorientation indicate progression of hypoglycaemia and requires immediate administration of glucose solution and food to restore blood glucose levels. Owners and veterinarians should be aware of Somogyi overswing which is a response to an overdose of insulin insufficient to cause an actual hypoglycaemia. As a partial hypoglycaemia begins to develop a hormonal response is triggered which results in release of glucose from hepatic glycogen stores. This results in rebound hyperglycaemia which may also manifest as glycosuria for part of the 24 hour cycle. There is a danger that the Somogyi overswing will be interpreted as a requirement for increase in the insulin dose rather than a decrease. This situation can progress to an overdose so large as to cause clinical hypoglycaemic effects.

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: QA10AC03

Pharmacotherapeutic group: Insulins and analogues for injection; intermediate acting.

4.2 Pharmacodynamics

Summary presentation of the active principle
The veterinary medicinal product is an intermediate acting insulin product containing porcine insulin, which is structurally identical to canine insulin. The active ingredient highly purified porcine insulin

is a naturally occurring hormone produced by the pancreas by the beta cells in the Islets of Langerhans. The overall effect of insulin is to promote an anabolic state in which there is a net synthesis of carbohydrate, protein and fat.
Insulin facilitates the intake of glucose obtained from food or gluconeogenesis by cells that are in need of energy supply for metabolism. Liver, adipose tissue and brain in particular utilise large amounts of glucose. In diabetes mellitus there is a decreased use of glucose caused by a relative or absolute insulin deficiency. Entrance of glucose into cells is therefore inhibited
and glucose accumulates in the body fluids.

4.3 Pharmacokinetics

The veterinary medicinal product is an intermediate acting product containing 35% amorphous insulin, which exerts an effect at about 3 hours after subcutaneous injection and has a duration of effect of about 6 - 8 hours, and 65% crystalline insulin which has a slower onset and a maximum effect between 7 - 12 hours after injection and a duration of 16 - 24 hours. In diabetic dogs, the action of the veterinary medicinal product in blood glucose concentrations, following subcutaneous administration peaks at about 4 - 8 hours post-injection and lasts for 14 - 24 hours. In diabetic cats the action of the veterinary medicinal product on blood glucose concentrations after subcutaneous administration peaks at about 4 - 6 hours and last for 8 - 12 hours post injection.

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: 24 months.
Vials: Shelf life after first opening the immediate packaging: 28 days.
Cartridges: Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Store unopened vials and cartridges upright in a refrigerator (2 °C – 8 °C).
Keep the vial or unopened cartridge in the outer carton.
Do not freeze. Protect from light.
Store in the original container.
After first opening, store below 25 °C and away from direct heat or direct light.
The pen containing a cartridge should not be stored in the refrigerator. The pen cap must be put back on the pen after each injection in order to protect from light.

5.4 Nature and composition of immediate packaging

Carton box with 1 or 10 glass vials of 2.5 ml with bromobutyl rubber stoppers and sealed with an aluminium caps.
Carton box with 1 glass vial of 10 ml with a bromobutyl rubber stopper and aluminium cap.
Carton box with 10 glass cartridges of 2.7 ml with a bromobutyl rubber plunger, a bi-layer bromobutyl and synthetic polyisoprene rubber stopper and aluminium cap.

Not all pack sizes may be marketed.

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

Intervet Ireland Limited.

7. MARKETING AUTHORISATION NUMBER(S)

VPA 10996/048/001

8. DATE OF FIRST AUTHORISATION

10/01/1997

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

26/01/2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).