

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Caninsulin 40 IU/ml Suspension for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Insulin* 40 IU

*(Porcine insulin present as approximately 30% amorphous Zinc insulin and 70 % crystalline Zinc insulin in a suspension)

Preservative: methylparahydroxybenzoate 0.1 % w/v.
For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

White to nearly white Suspension for injection

4. CLINICAL PARTICULARS

4.1. Target species

Dogs and cats

4.2. Indications for use, specifying the target species

The product is an intermediate acting insulin product containing porcine insulin, which is structurally identical to canine insulin. It is indicated in cases of diabetes mellitus (insulin deficiency) in dogs and cats, where the required blood levels are achieved by using an individually adjusted dose of the product.

4.3. Contra-indications

The product must not be administered by the intravenous route
The product is a medium duration insulin and is not intended for the treatment of animals with severe acute diabetes presenting in a ketoacidotic state.

4.4. Special warning for each target species

In the cat diabetic remission is possible.

4.5. Special precautions for use

i) Special precautions for use in animals

Before the product is administered owners should be instructed to have a box of powdered glucose at home. 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.

Polyuria, polydipsia and polyphagia in combination in chronic cases with weight loss, general bad condition, loss of hair or abnormal furry coat and lethargy are the most common clinical symptoms of hyperglycaemia and require administration of insulin to restore blood glucose levels to the normal range.

The use of progestagens (oestrus inhibitors) in patients suffering from diabetes mellitus should be avoided.

Stress and irregular extra exercise must be avoided. Care must be taken with the use of corticosteroids. Ovariohysterectomy may have to be considered.

It is important to establish a strict feeding schedule in consultation with the owner which will include a minimum of fluctuations and changes.

Administration of the product must be carried out by an adult responsible for the welfare of the animal.

The product must be administered with specific U-40 sterile single-use syringes (vial) or with VetPen (cartridge).

ii) Special precautions to be taken by the person administering the medicinal product to animals

Accidental self-injection can provoke clinical signs of hypoglycaemia and there is a low possibility of an allergic reaction. In case of accidental self-injection seek medical advice immediately and show the package insert to the doctor.

In the unlikely event of accidental eye and skin contact, wash the area with clean, running water.

4.6. Adverse reactions (frequency and seriousness)

Local injection site reactions have been reported rarely in dogs and very rarely in cats. These reactions are usually mild and reversible. In very rare cases, allergic reactions to porcine insulin have been reported.

4.7. Use during pregnancy, lactation or lay

The use of the product is not contra-indicated during pregnancy or lactation but requires close veterinary supervision to account for changes in metabolic requirements during this period.

4.8. 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, progestogens, amitraz and alpha-2 agonists, such as medetomidine, dexmedetomidine, xylazine. Monitoring of glucose concentrations should be used to adjust the dose accordingly.

Similarly, changes in diet or exercise may alter insulin requirements.

4.9. Amounts to be administered and administration route

Caninsulin should be administered once or twice daily, as appropriate, by subcutaneous injection. Alternate the injection site daily. Before first use shake the vial thoroughly until a homogeneous, uniformly milky suspension is obtained. Foam on the surface of the suspension formed during shaking should be allowed to disperse before the product is used and, before each subsequent use, the product should be gently mixed to maintain a homogeneous, uniformly milky suspension before use. Agglomerates can form in insulin suspensions: do not use the product if visible agglomerates persist after shaking thoroughly

Vial: Before each use, invert the vial a few times before use until a homogenous suspension is obtained. A 40 IU/ml insulin syringe should be used.

Cartridge: Before each use, invert the vial a few times before use until a homogenous suspension is obtained. The cartridge is designed to be used with VetPen. VetPen is accompanied by a package leaflet with detailed instruction for use to be followed. The injection procedure when using VetPen is as follows:

1. Peel the protective film from a new pen needle. Screw the pen needle straight onto the cartridge holder. Remove the outer protective needle cap from the pen needle.

Replace the pen cap onto the insulin pen. Turn the pen up and down at least 10 times.

2. **It is important to remove the air from the cartridge (prime the pen) before use to avoid injection of air and ensure proper dosing. Dial 1 unit on the dose selector. Remove the pen cap and the needle cap.**

Position the pen carefully with the needle pointing vertically upwards. Tap the cartridge gently with your finger a few times to push any air bubbles to the top of the cartridge. Push and hold the release button towards the needle until the arrow (▶) on the pen body points to the start line (—) on the dose selector.

A small amount of insulin may appear at the needle tip before the pen is fully primed. Repeat steps 1 and 2 until insulin drips actively or squirts out of the needle tip.

Confirm that the pen is fully primed by ensuring that the air bubble is no longer visible in the cartridge window during inversion. The insulin pen is now primed and ready for use.

3. Make sure the arrow (▶) on the pen body points to the start line (—) on the dose selector. If it does not, please refer to 'Priming Advice' on the leaflet supplied with the VetPen.

4. Dial up the number of units required per your veterinary surgeon's direction. **Never attempt to forcefully dial back the dose selector, as doing so may damage the insulin pen and result in inaccurate dosing. If at any time you select too high a dose, we recommend that the incorrect dose is fully expelled into a safe place and the required dose is redialed. Make sure before injecting that the arrow (▶) points towards the correct number of units on the dose selector.**

5. The injection should be performed subcutaneously, 2 to 5 cm ($\frac{3}{4}$ to 2 in) from the dorsal midline, varying from behind the scapulae (shoulder) to the mid-lumbar

region (mid-back) and alternating sides. Insert the needle using the injection technique recommended by your veterinary surgeon then push the release button towards the pen needle and hold it in place until the start line on the dose selector returns to the arrow on the pen body (▶—).

Releasing the button prematurely will result in incomplete delivery of the dose. After the start line returns to the arrow, wait for a **minimum of 5 seconds** before removing the needle from the skin.

If the needle is removed or dislodged from the skin too early, you may observe small drops of insulin leaking from the needle, which can result in incomplete dosing. If this occurs, do not attempt to re-dose. Wait and give your pet its usual dose at the next injection.

If the dose selector stops before the start line on the dose selector (—) returns to the arrow on the pen body (▶), this indicates that your pet has not received a full dose. If only a partial dose is administered, do not attempt to re-dose. Wait and give your pet its usual dose at the next injection.

When changing between dosing devices (syringes or VetPen), owners should be advised to monitor their animal closely to detect any changes in behavior or clinical condition. A dose adjustment may be required.

A once daily injection is sufficient to reduce the blood glucose concentration in most diabetic dogs. However, the duration of action may vary, making it necessary to administer the insulin dose twice daily to some diabetic dogs.

In diabetic cats, it is necessary to administer Caninsulin 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

Dog: Insulin therapy is initiated with the starting dose of **0.5 to 1.0 IU/kg** bodyweight once daily, rounded down to the lowest entire number of units.

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 days.

The duration of insulin action as determined by blood glucose curve, may require treatment to be administered twice daily. 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 new doses should be administered at 12-hour intervals. Further dose adjustments should be made progressively as previously explained. Following switching to twice daily dosing, it is recommended that the clinical signs and blood glucose response be monitored closely.

To achieve a balance between the generation of glucose and the effect of the

product, feeding should be synchronized 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 coincides with Caninsulin administration. Each meal should be fed at the same time each day.

Cat: The initial dose is **1 IU or 2 IU** 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)	1 IU twice daily
≥20 mmol/l or ≥ 3.6 g/l (≥360 mg/dl)	2 IU twice daily

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. 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 stabilized, a long term management program needs to be established. The aim should be to manage the animal in such a way as to minimize the variations in its insulin requirement. This includes clinical monitoring to detect under or over dosage of insulin and adjustment of dose if required. Careful stabilization 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 biochemical parameters (like blood glucose and/or fructosamine concentration). 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 recognize the signs of hypo- or hyperglycaemia and respond appropriately is very important.

4.10. Overdose (symptoms, emergency procedures, antidotes), if necessary

Before the product is administered owners should be instructed to have a box of powdered glucose at home. Signs of hunger, increasing anxiety, unstable locomotion, muscle twitching, stumbling or sinking in the rear legs and disorientation indicate progression of hypoglycaemia and require immediate administration of glucose solution and food to restore blood glucose levels.

4.11. Withdrawal period(s)

Not applicable

5. PHARMACOLOGICAL PROPERTIES

Active ingredient: porcine insulin highly purified

Pharmacotherapeutic group: antidiabetic

ATCvet code: QA10AC03 (Drugs used in Diabetes and Analogues for injection, intermediate-acting, Insulin (pork)).

5.1. Pharmacodynamic properties

Summary presentation of the active principle

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.

In diabetic dogs, the action of Caninsulin 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 Caninsulin on blood glucose concentrations after subcutaneous administration peaks at about 4-6 hours and last for 8-12 hours post injection.

5.2. Pharmacokinetic particulars

The product is an intermediate acting product containing 30% 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 70% crystalline insulin which has a slower onset and a maximum effect between 7 - 12 hours after injection and a duration of 16-24 hours.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Methylparahydroxybenzoate 0.1 % w/v.
Zinc chloride
Sodium acetate trihydrate
Sodium chloride
Hydrochloric acid or Sodium hydroxide (for pH adjustment)
Water for injections

6.2. Major incompatibilities

None known

6.3. Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years
Shelf life after first opening of the immediate packaging: 28 days.

6.4. Special precautions for storage

Store upright and refrigerated between + 2 and + 8 °C. Protect from light. Do not freeze.

After first opening store refrigerated at between + 2 and + 8 °C.

6.5. Nature and composition of immediate packaging

Cardboard box with 5 or 10 glass vials (Ph.Eur. Type I) of 2.5 ml with a rubber stopper and aluminium cap, or a cardboard box with 1 glass vial (Ph.Eur. Type I) of 10 ml with a rubber stopper and aluminium cap.

2.7 ml glass Type I cartridge with two sterile colourless Type I glass beads 2.4-2.5 mm in diameter. Closed with a red, 10 mm bromobutyl rubber plunger on the bottom, and with a gold coloured, 7.5 mm bi-layer bromobutyl rubber/polyisoprene stopper and an aluminium crim cap on top. Available in boxes of 10 x 2.7 ml cartridges.

The glass cartridge is designed to be used with the injector VetPen 8 or VetPen 16. Not all pack sizes may be marketed.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MSD Animal Health UK Limited
Walton Manor
Walton
Milton Keynes
Buckinghamshire
MK7 7AJ

8. MARKETING AUTHORISATION NUMBER

Vm 01708/4244

9. DATE OF FIRST AUTHORISATION

8 December 1992

10. DATE OF REVISION OF TEXT

October 2020

Approved 27 October 2020

A handwritten signature in black ink, appearing to read "Hunter.", is written below the approval date. The signature is stylized and includes a large, looped initial.