

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Petsulin Protamine Zinc Solution for Injection
Protamine Zinc Insulin Injection BP 100 iu/ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<u>Qualitative composition</u>	<u>Quantitative composition</u>
Active substance Insulin Crystalline Bovine	100 iu/ml
Excipients Phenol	0.065 % w/v

For a full list of excipients, see section 6.1.

PHARMACEUTICAL FORM

3.

Solution for injection.
White, sterile suspension, pH 6.9 to 7.8.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs and cats.

4.2 Indications for use, specifying the target species

For the treatment of type 1 insulin-dependent diabetes mellitus in the dog and cat only. The product has a medium to extended duration of action when administered subcutaneously, and is used to treat uncomplicated (non-ketoacidotic) cases of insulin dependent diabetes mellitus.

4.3 Contraindications

Hypoglycaemia.

4.4 Special warnings for each target species

As a general rule the control of diabetes in dogs and cats should be reassessed once or twice a year or whenever there is a weight loss of > 10 % and a healthy appetite. Reassessment is particularly important in cats in which diabetes may sometimes resolve or enter a period of remission.

During reassessment blood glucose must be monitored frequently. If the concentration exceeds 2.5 mg/ml, an increase in the insulin dose is indicated. If, at its lowest point blood, glucose concentration is below 0.8 mg/ml, then the dose should be decreased, even if at other times the animal may be slightly hyperglycaemic. Usually an alteration in the insulin dosage of 10-20 % either way is sufficient to regain control.

If an animal appears to be insulin resistant, that is to say is hyperglycaemic in spite of receiving 2.2 units/kg, the case should also be reassessed, particularly in relation to the owner's competency and injection technique.

4.5 Special precautions for use

i. Special precautions for use in animals

Insulin requirements may vary with illness, stress, pregnancy, exercise or changes in diet. The animal's diet must be modified, adjusted and controlled. This is easier to accomplish in dogs than cats. The calorific intake should be adjusted to maintain ideal bodyweight. It should take into account also the animal's exercise pattern. The diet should contain additional fibre (15 % cellulose or pectin), 50 % digestible carbohydrate and 10-15 % fat. Specially prepared diets (tinned and dry food) for diabetic dogs and cats are available commercially.

Insulin requirements may decrease with liver or kidney disease or when drugs with hypoglycaemic activity are given.

ii. Special precautions for the person administering the veterinary medicinal product to animals

Care should be taken to avoid accidental self-injection. In the event of accidental self-injection, medical advice **MUST** be sought immediately showing the doctor the label.

Persons who are hypersensitive (allergic) to insulin or other ingredients in this product should wear impermeable rubber gloves, when handling this product.

Avoid contact with skin and eyes. In the event of accidental eye or skin contact, wash/irrigate the area with clean running water. Seek medical attention if irritation persists.

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

If excessive levels of insulin are administered, blood glucose will fall rapidly. Physiological responses bring about a compensatory increase (Somogyi overswing). Veterinary surgeons should consider this when animals apparently require excessive doses of insulin.

Overdose may result in hypoglycaemic shock.

Underdose may result in hyperglycaemia.

4.7 Use during pregnancy, lactation or lay

The requirements for insulin will vary and dose adjustment will be necessary.

4.8 Interaction with other medicinal products and other forms of interaction

Certain types of medication including corticosteroids, thyroxine and sympathomimetic agents, may increase insulin requirements. Adrenocorticotrophic hormone has resulted in insulin resistance in dogs.

4.9 Amount(s) to be administered and administration route

It is recommended that 0.5 ml, 100 unit/ml insulin sterile disposable syringes are used for administration and that a new sterile syringe and needle is used for each injection.

The vial should be mixed gently by inversion several times before the dose is withdrawn. The vial must not be used if the contents do not redisperse. Injections should be made immediately upon withdrawal from the vial.

The higher end of the dose range is more suitable for the long acting forms. The initial dose range for dogs is 0.5-1.1 units/kg, and 10-15 units/dog by subcutaneous injection. Recommended fine tuning increments fall within the range 0.5-3 units/dog. The corresponding figures for cats are 0.2-0.5 units/kg, 1-3 units/cat and 0.5 units/cat respectively by subcutaneous injection.

A summary of recommendations incorporating feeding rations (which are fed within the hour before injection, whether the animal is fed once or twice daily) is as follows:

Dog: Initial dose: 0.5 units/kg (am)
Frequency: Once daily
Feeding: 67 % in am, 33 % in pm
Adjustment: 1-3 units/kg/dog

Cat: Initial dose: 0.5 units/kg (am)
Frequency: Once or twice daily
Feeding: 50 % in am, or free choice
Adjustment: 0.5 units/cat/dose

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

Symptoms: Overdosage causes hypoglycaemia. (Progressively anorexia, lassitude, nervousness, coma and death).

Treatment: Veterinary advice should be sought at the earliest opportunity. Hypoglycaemia should be treated immediately with the administration of 50-20 g glucose orally or parenterally, or a slow intravenous infusion of 5 % dextrose infusion started. The insulin dose should be reduced 25-50 %. If the animal is at home and convulsing, sugar water or syrup should be carefully introduced into the animal's mouth until the convulsions stop.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group:

Insulin (beef)

ATC Vet Code:

QA10AC02

5.1 Pharmacodynamic properties

Insulin is a protein hormone produced and secreted by the Islets of Langerhans within the pancreas. It has the effect of reducing the level of glucose in the bloodstream, and acts in concert with glucagon, which has the opposite effect to maintain normoglycaemia.

The essential immediate cause of diabetes is partial or complete insulin deficiency. The greater part of the pancreas is exocrine, secreting digestive enzymes into the small intestine via the common bile duct. Dispersed throughout the pancreas are Islets of Langerhans - the endocrine pancreas. The Islet β cells secrete stored insulin in response to a number of stimuli; blood glucose, glucagon, gastrointestinal peptide hormone, amino and fatty acids, systemic chemical messengers (acetylcholine and β agonists) and some medicines (sulphonylureas).

Insulin plays a key role in the regulation of carbohydrate, fat and protein metabolism. A relative or absolute deficiency of insulin decreases the utilisation of glucose, amino and fatty acids especially by liver, muscle and fat cells. The α_2 Islet cells secrete glucagon, a small polypeptide hormone with action essentially opposite to insulin. Its main actions are glycogenolysis and gluconeogenesis. Insulin, glucagon from Islet α_1 and α_2 cells and growth hormone (from the hypothalamus) are of central importance to the regulation of intermediary metabolism.

The main precipitating factors of diabetes are not known. There are some fairly obvious factors such as neoplasia, pancreatitis and genetics. Whatever the cause, the pathology is well established. There is progressive destruction of the endocrine pancreas-hyaline degeneration, fibrosis, tumour cell infiltration and, in cats, amyloid deposition. The majority of dogs and cats suffering from diabetes require exogenous insulin if they are to survive and return to good health.

5.2 Pharmacokinetic properties

Protamine zinc insulin (PZI) is made by combining amorphous insulin with buffered protamine to form a precipitate, then adding small amounts of zinc. It is very slowly absorbed from the site of injection. It has a lower and delayed peak concentration but a longer duration of activity compared to neutral insulin. Mean peak activity time is 12 ± 4 hours. Activity persists for at least 24 hours.

Consequently diabetes in dogs can be controlled using a single dose PZI injection. Naturally, because of the significantly different pharmacokinetics, a higher dose of long acting insulin has to be used.

In cats, mean peak activity time is 4 ± 1 hour after a subcutaneous injection of PZI. Activity persists for at least 14 hours. However substantial individual animal variations have been observed. Whereas diabetes in some cats will be well regulated with a single daily subcutaneous PZI injection, twice daily injection may be required for others.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol
Protamine sulfate
Disodium phosphate dodecahydrate
Zinc (as zinc chloride)
Glycerol
Hydrochloric acid, dilute, phosphoric acid or sodium hydroxide solutions (for pH adjustment)
Water for injections

6.2 Incompatibilities

The mixing of Petsulin Neutral and Petsulin Protamine Zinc in the syringe not recommended.

6.3 Shelf life

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

6.4 Special precautions for storage

Store in a refrigerator (+2 to 8°C).
Protect from freezing.
Following withdrawal of the first dose, use product within 28 days.
Discard unused material.

6.5 Nature and composition of immediate packaging

10 ml neutral glass vial sealed with a grey chlorobutyl or red bromobutyl rubber bung and aluminium overseal.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products, if appropriate

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

7. MARKETING AUTHORISATION HOLDER

Dechra Limited
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ST7 1XW
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8. MARKETING AUTHORISATION NUMBER

Vm 10434/4001

9. DATE OF FIRST AUTHORISATION

02/07/2004

10. DATE OF REVISION OF THE TEXT

13/08/2008