ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ProZinc 40 IU/ml suspension for injection for cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

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

One IU (International Unit) corresponds to 0.0347 mg of insulin human.
*produced by recombinant DNA technology

Excipients:

Protamine sulfate	0.466 mg
Zinc oxide	0.088 mg
Phenol	2.5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
Cloudy, white, aqueous suspension.

4. CLINICAL PARTICULARS

4.1 Target species

Cats

4.2 Indications for use, specifying the target species

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

4.3 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.

4.4 Special warnings for each target species

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

4.5 Special precautions for use

Special precautions for use in animals
The insulin dose may need to be adjusted or discontinued in case of remission of the diabetic state.
After the daily insulin dose is established, regular glucose monitoring is recommended.
Treatment with insulin can cause hypoglycaemia, for clinical signs and appropriate treatment, see

section 4.10.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Accidental self-injection can provoke clinical signs of hypoglycaemia and 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 to the physician.

4.6 Adverse reactions (frequency and seriousness)

Hypoglycaemic reactions were very commonly (13% (23 of 176) of treated cats) observed during a safety and efficacy study. These reactions were generally mild in nature. Clinical signs may include hunger, anxiety, unstable locomotion, muscle twitching, stumbling or sinking in the rear legs and disorientation.
In this case immediate administration of a glucose solution and/or food is required.

Insulin administration should be temporarily stopped and the next dose of insulin adjusted appropriately.
Local injection site reactions were very rarely reported and resolved without cessation of therapy.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reactions)
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

The safety and efficacy of ProZinc in breeding, pregnant and lactating cats has not been evaluated.
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.

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 (e.g. corticosteroids and gestagens). Monitoring of glucose concentrations should be performed to adjust the dose accordingly. Similarly, feeding a high protein/low carbohydrate diet may alter insulin requirements (e.g. decrease of insulin dose).

4.9 Amounts to be administered and administration route

Subcutaneous use.

Dosage:
The initial recommended dose is 0.2 to 0.4 IU/kg bodyweight every 12 hours. For cats previously controlled on insulin, a higher starting dose up to 0.7 IU/kg bodyweight may be appropriate.

The veterinarian should re-evaluate the cat 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. Adjustments of insulin dose if

required should usually be done between 0.5 to 1 IU per injection. Dose reductions due to observed hypoglycaemia or suspected Somogyi effect (rebound hyperglycaemia) may be of 50% or higher.

Once adequate glycaemic control is achieved regular blood glucose control (e.g. every 3 to 4 months or more often) should be performed and further adjustments in the insulin dose might be necessary.

Cats can develop diabetic remission, in which case sufficient endogenous insulin production will be regained and 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 twice daily by subcutaneous injection.
Avoid introduction of contamination during use.
After gently rolling the vial, ProZinc 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 product.
Agglomerates (e.g. clumps) can form in insulin suspensions: do not use the product if visible agglomerates persist after gently rolling the vial.

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

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

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Insulins and analogues for injection, intermediate acting.
ATCvet code: QA10AC01 Insulin (human).

5.1 Pharmacodynamic properties

Insulin activates insulin receptors and therewith a complex cell signaling 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.

Under clinical field conditions in diabetic cats the maximal action on blood glucose concentrations (e.g. blood glucose nadir) after subcutaneous administration was observed at a mean of 6 hours (range 3 to 9 hours). In the majority of cats the glucose lowering effect lasted for a minimum of 9 hours after first insulin injection.

5.2 Pharmacokinetic particulars

Absorption:
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.

Metabolism:
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. Fourty per cent of insulin is eliminated by the liver and 60% is eliminated by the kidney.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Protamine sulfate
Zinc oxide
Glycerol
Dibasic sodium phosphate, heptahydrate
Phenol
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Major incompatibilities

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

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: 60 days.

6.4 Special precautions for storage

For unused and broached vials:
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.

6.5 Nature and composition of immediate packaging

Pack size of one clear glass vial of 10 ml.
The vial is closed with a butyl rubber stopper and sealed with a plastic flip-off cap.

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

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

Boehringer Ingelheim Vetmedica GmbH
Binger Strasse 173
55216 Ingelheim/Rhein
GERMANY

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/152/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12/07/2013
Date of last renewal:

10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY OR USE

C. STATEMENT OF THE MRLs

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release
Boehringer Ingelheim Vetmedica GmbH
Binger Strasse 173
55216 Ingelheim/Rhein
GERMANY

KVP Pharma + Veterinär Produkte GmbH
Projensdorfer Str. 324
24106 Kiel
GERMANY

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton for 10 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ProZinc 40 IU/ml suspension for injection for cats
insulin human as protamine zinc insulin

2. STATEMENT OF ACTIVE SUBSTANCES

40 IU/ml of insulin human

3. PHARMACEUTICAL FORM

Suspension for injection

4. PACKAGE SIZES

1 x 10 ml

5. TARGET SPECIES

Cats

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

10. EXPIRY DATE

EXP {month/year}
Once broached use within 60 days.

11. SPECIAL STORAGE CONDITIONS

Store upright in a refrigerator.
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
GERMANY

16. MARKETING AUTHORISATION NUMBERS

EU/2/13/152/001

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial, 10 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ProZinc 40 IU/ml injection for cats
insulin human as protamine zinc insulin

2. QUANITITY OF THE ACTIVE SUBSTANCE(S)

40 IU/ml

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

10 ml

4. ROUTE(S) OF ADMINISTRATION

SC

5. WITHDRAWAL PERIOD

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}
Once broached use by ...

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
ProZinc 40 IU/ml suspension for injection for cats

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:
Boehringer Ingelheim Vetmedica GmbH
Binger Strasse 173
55216 Ingelheim/Rhein
GERMANY

Manufacturer responsible for batch release:
KVP Pharma + Veterinär Produkte GmbH
Projensdorfer Str. 324
24106 Kiel
GERMANY

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

ProZinc 40 IU/ml suspension for injection for cats
insulin human

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENTS

Each ml contains:

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

One IU (International Unit) corresponds to 0.0347 mg of insulin human.
*produced by recombinant DNA technology

Excipients:
Protamine sulfate 0.466 mg
Zinc oxide 0.088 mg
Phenol 2.5 mg

Cloudy, white, aqueous suspension.

4. INDICATION(S)

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

5. 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.

6. ADVERSE REACTIONS

Hypoglycaemic reactions were very commonly (13% (23 of 176) of treated cats) observed during a safety and efficacy study. These reactions were generally mild in nature. Clinical signs may include hunger, anxiety, unstable locomotion, muscle twitching, stumbling or sinking in the rear legs and disorientation.
In this case immediate administration of a glucose solution and/or food is required.

Insulin administration should be temporarily stopped and the next dose of insulin adjusted appropriately.
Local injection site reactions were very rarely reported and resolved without cessation of therapy.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reactions)
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Cats

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Subcutaneous use.

Dosage:
The initial recommended dose is 0.2 to 0.4 IU/kg bodyweight every 12 hours. For cats previously controlled on insulin, a higher starting dose up to 0.7 IU/kg bodyweight may be appropriate.

The veterinarian should re-evaluate the cat 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. Adjustments of insulin dose if required should usually be done between 0.5 to 1 IU per injection. Dose reductions due to observed hypoglycaemia or suspected Somogyi effect (rebound hyperglycaemia) may be of 50% or higher.

Once adequate glycaemic control is achieved regular blood glucose control (e.g. every 3 to 4 months or more often) should be performed and further adjustments in the insulin dose might be necessary.

Cats can develop diabetic remission, in which case the cat's own insulin production is regained and insulin dosing will need to be adjusted or ceased.

Method of administration:
The veterinary medicinal product should be administered twice daily by subcutaneous injection.

9. ADVICE ON CORRECT 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.
Particular care should be taken with regard to the accuracy of dosing.
The dose should be given concurrently with or immediately after a meal.
Avoid introduction of contamination during use.
After gently rolling the vial, ProZinc 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 product.
Agglomerates (e.g. clumps) can form in insulin suspensions: do not use the product if visible agglomerates persist after gently rolling the vial.

10. WITHDRAWAL PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

For unused and broached vials:
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.
Shelf life after first opening the container: 60 days.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton and the vial after EXP.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Very stressful events, concomitant treatment with gestagens and corticosteroids or other concomitant diseases (e.g. infectious or inflammatory or endocrine diseases), might influence insulin effectiveness and therefore the insulin dose may need to be adjusted.

Special precautions for use in animals:
The insulin dose may need to be adjusted or discontinued in case of remission of the diabetic state.
Cats can develop diabetic remission, in which case the cat's own insulin production is regained.
After the daily insulin dose is established, regular glucose monitoring is recommended.

Treatment with insulin can cause hypoglycaemia, for clinical signs and appropriate treatment, please refer to section “Overdose”, below.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Accidental self-injection can provoke clinical signs of hypoglycaemia and 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 to the physician.

Pregnancy and lactation:
The safety and efficacy of ProZinc in breeding, pregnant and lactating cats has not been evaluated.
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.

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, feeding a high protein/low carbohydrate diet may alter insulin requirements (e.g. decrease of insulin dose).

Overdose (symptoms, emergency procedures, antidotes):
An overdose of insulin can result in hypoglycaemia in which case immediate administration of a glucose solution 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.

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

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed via wastewater or household waste. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

15. OTHER INFORMATION

Pack size of 1 clear glass vial of 10 ml. The vial is closed with a butyl rubber stopper and sealed with a plastic flip-off cap.