IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Tranquiline 35 mg/ml Oral Gel for Dogs

PRODUCT SUMMARY

EU Procedure number	IE/V/0278/001/DC
Name, strength and pharmaceutical form	Tranquiline 35 mg/ml Oral Gel for Dogs
Active substance(s)	Acepromazine (as acepromazine maleate)
Applicant	Floris Holding BV Kempenlandstraat 33 5262 GK Vught Netherlands
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of procedure	23/11/2011
Target species	Dogs
Indication for use	For sedation and anaesthetic pre-medication. Neuroleptanalgesia in combination with a morphine derivative. Anti-emetic effect, symptomatic therapy in case of vomiting and motion sickness.
ATCvet code	QN05AA04
Concerned Member States	AT, BE, BG, CY, DE, DK, EL, ES, FR, IT, NL, NO, PL, RO, SE, UK

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.
The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

The product is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.

It has been shown that the product can be safely used in the target species.
The product is safe for the user, and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.

The efficacy of the product was demonstrated according to the claims made in the SPC.

The overall benefit-risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition
The product contains 35 mg/ml of the active substance acepromazine (47.50 mg/ml as acepromazine maleate) and excipients

methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), sodium acetate trihydrate, sodium cyclamate (E952), hydroxyethylcellulose, glycerol (E422) and purified water.
The product is presented in an oral dosing syringe which is graduated at 1 ml intervals.
The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product
The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.
Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials
The active substance is acepromazine maleate, an established active substance described in the BP (vet). The active substance is manufactured in accordance with the principles of good manufacturing practice.
The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies
There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

E. Control on intermediate products
Not applicable

F. Control Tests on the Finished Product
The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product.
Satisfactory validation data for the analytical methods have been provided.
Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

G. Stability
Stability data on the active substance acepromazine maleate has been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.
Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

H. Genetically Modified Organisms
Not applicable.

J. Other Information
Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing
The application for Tranquiline 35 mg/ml Oral Gel for Dogs was submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended (a generic application). The reference product is Sedalin Oral Gel 3.5% w/v which has been authorised in the RMS for not less than 10 years (VPA 10966/024/001).
Given that bioequivalence with an authorised reference product is claimed, pharmacological or basic toxicological data were not presented. For this information, the applicant cross-referred to the authorised reference product. The claim for bioequivalence with the reference product is accepted.
User Safety
The applicant provided a user safety assessment conducted in accordance with current guidance, which identified the main exposure situations and risks arising from use of the product, in particular the risks to the user in the event of accidental oral exposure given that the active substance is a central nervous system depressant. On the basis of the information provided, it was concluded that the product does not present an unacceptable risk to the user when used in accordance with label recommendations. Furthermore, given that bioequivalence with the reference product is claimed, and that the generic product is presented in the same dose volume and similar dosing device as the reference product, the risk to the user is considered to be the same as that posed by the reference product. Given that this veterinary medicinal product is presented in prefilled

syringe and in glass bottle the following precautions to be taken by the person administering the veterinary medicinal product have been agreed and included in the product literature:
- Acepromazine may cause sedation. Care should be taken to avoid accidental ingestion.
- To avoid accidental ingestion by a child when using the prefilled syringe: replace cap immediately after use. Keep the broached oral syringe in the original carton and make sure that the carton is closed properly. To avoid accidental ingestion by a child when using the glass bottle, do not leave the filled syringe unattended and store the properly closed bottle and used syringe in the original carton.
- This product must be used and kept out of sight and reach of children.
- In case of accidental ingestion, seek medical advice immediately informing the health professionals of phenothiazine poisoning. Show the package leaflet or the label to the doctor.
- DO NOT DRIVE as sedation and changes in blood pressure may occur.
- People with known hypersensitivity to acepromazine or other phenothiazines or to any of the excipients should avoid contact with the veterinary medicinal product.
- Persons with sensitive skin or in frequent contact with the product are advised to wear impermeable gloves.
- Wash hands and exposed skin thoroughly after use.
- In case of accidental spillage onto the skin, immediately after exposure wash the exposed skin with large amounts of water.
- This product may cause mild eye irritation. Avoid contact with eyes. If accidental eye contact occurs, flush gently with running water for 15 minutes and seek medical advice if any irritation persists.

Ecotoxicity

The applicant presented a first phase environmental risk assessment for the product. In accordance with the relevant guideline, the ERA concluded at Phase I on the grounds that the product is for use in non-food animals only. No further assessment is required.
It is accepted that Tranquiline 35 mg/ml Oral Gel for Dogs does not present a risk to the environment when used as recommended.

III.B Residues documentation

Residue Studies
As the product is proposed for use in companion animals, no residue data were presented.

IV. CLINICAL ASSESSMENT

The application for Tranquiline 35 mg/ml Oral Gel for Dogs was submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended (a generic application). The reference product is Sedalin Oral Gel 3.5% w/v which has been authorised in the RMS for not less than 10 years (VPA 10966/024/001).

Exemption from the need to conduct bioequivalence studies is claimed, therefore, preclinical or clinical studies were not presented, and the applicant cross-referred to the reference product for these sections of the dossier.
The proposed exemption from the need to conduct bioequivalence testing in accordance with current guidance is accepted, on the basis that:

- the product is an oral solution, syrup or other similarly solubilised form.
- it contains an active substance in the same concentration as a product approved for use in the target species that is the subject of the new application.
- it contains no inactive substance that can significantly affect the absorption of the active substance.

Although the reference and test products are not oral solutions or syrups, given that the gel is water-based with the active substance completely dissolved in aqueous solution and is the same pharmaceutical form as the reference product, it is accepted that an oral gel can be considered as an 'other similarly solubilised form'. The generic product contains an active substance in the same concentration as the reference product (35 mg/ml acepromazine), the excipients are qualitatively the same as the reference product and there are no excipients present that could significantly affect the absorption of the active substance.
The RMS accepts the claim for bioequivalence with the reference product, and thus the omission of pre-clinical and clinical studies is accepted.

The reference product is authorised for use both in dogs and in horses not intended for human consumption. Tranquiline 35 mg/ml Oral Gel for Dogs is for use in dogs only. The indications and posology proposed for Tranquiline 35 mg/ml Oral Gel for Dogs are as follows:

Indication:

For sedation and anaesthetic pre-medication.
Anti-emetic effect, in case of vomiting associated with motion sickness.

Dosage:
The product is intended for oral administration according to the following dosage guidelines:

Light sedation: 1.0 mg acepromazine / kg body weight
Deeper sedation: 2.0 mg acepromazine / kg body weight
Pre-medication: 3.0 mg acepromazine /kg body weight
Anti-emetic effect: 1.0 mg/kg body weight
The dose to be administered to dogs weighing ≥35 kg should not be more than 1 mg/kg for any level of sedation/premedication.

Prefilled syringe
The product is filled into a 10 ml polyethylene syringe. The flanged plunger has a locking ring which should be adjusted to supply the volume required in accordance with the dosage guidelines. 1.0 ml intervals are printed on the syringe plunger, but the plunger is indented/flanged at intervals of 0.5 ml. A single turn of the locking ring will move the ring backwards allowing a dose volume of 0.5 ml to be expelled. Two turns of the locking ring will supply a dose volume of 1.0 ml. Three turns of the locking ring are required for a dose of 1.5 ml.
The syringe is brought into the animal's mouth and the appropriate dose is expelled into the animal's cheek.
The gel can also be mixed with food.

Glass bottle
The product is filled into 10 ml glass bottles with child resistant closure and supplied with a syringe with a dose graduation allowing accurate dosing. The 1 ml syringe can administer 0.05 to 1.0 ml with 0.05 ml increments. Withdraw the appropriate dose from the bottle using the supplied syringe. The syringe is brought into the animal's mouth and the appropriate dose is expelled into the animal's cheek.
Some product will remain in the glass bottle, i.e. is not extractable.
The gel can also be mixed with food.

V. OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

VI. POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the HPRA website.

This section contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

Changes:
Given that a new product presentation (10 ml glass bottle) was authorised, the user safety and amounts to be administered were updated.