IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Z-Itch 40 mg/ml pour-on solution

PRODUCT SUMMARY

EU Procedure number	IE/V/0626/001 (formerly UK/V/0477/001)
Name, strength and pharmaceutical form	Z-Itch
Active substances(s)	Permethrin (80:20) technical
Applicant	Floris Holding BV, Kempenlandstraat 33, 5262 GK Vught, Netherlands
Legal basis of application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Date of Authorisation	20 March 2013 (UK) 21 June 2013 (IE)
Target species	Donkey,Non food-producing horses
Indication for use	For the control of the biting insect *Culicoides* spp. This product may be used as an aid in the control of sweet itch.
ATCvet code	QP53AC04
Concerned Member States	Ireland, UK CMS Wave 1: UK CMS Wave 2: BE, DE, SE CMS Wave 3: IT, PL, PT CMS Wave 4: DK

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

Z-itch 40 mg/ml Pour-on Solution is a generic product based on the reference product Young's Swift. Bioequivalence is claimed with the reference product, authorised in the UK since 1985, but not currently marketed. The reference product currently marketed in the UK, a copycat of the originator product, is Switch 4% w/v Pour-On Solution.

Z-Itch 40 mg/ml Pour-On Solution contains permethrin [80:20] technical. The product is indicated for use in horses and donkeys, to aid in the control of sweet itch. The recommended dose is 4 mg/kg (1 ml/10 kg body weight), up to a maximum of 40 ml. The dose is administered to the mane and rump areas in two equal amounts. The dose is administered at the commencement of the sweet itch season and repeated as required. A once a week treatment is normally sufficient.

The cause of sweet itch is thought to be hypersensitivity to the bites of insects, for example *Culicoides* species. For severe cases and for cases which do not respond to treatment, veterinary advice should be sought. The product is contraindicated in horses and donkeys intended for human consumption and should not be applied to the saddle area.

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 slight reactions observed are indicated in the SPC.

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 the active substance permethrin (80:20) technical and the excipient butyl dioxitol.

The container/closure system consists of 250 ml of the product in a high density polyethylene container and closed with a white, polypropylene screw fit cap with a heat induction seal. The 'squeeze and pour' bottles also have an integral dispensing chamber calibrated at 5 ml, 6 ml and 10 ml graduations. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation is justified. 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. The manufacturing process is straightforward. The permethrin is heated for several hours before being dissolved by mixing it into a portion of the butyl dioxitol. The remaining volume is made up by continuing to add the butyl dioxitol and mixing, before filling the containers with the product.

C. Control of Starting Materials
The active substance is permethrin (80:20) technical, an established active substance not described in the European Pharmacopoeia (Ph. Eur). Data on the active substance are supplied in the form of an Active Substance Master File. 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.

The excipient, butyl dioxitol, is an established substance not described in a pharmacopeia. The substance has been used in similar products for many years. An in-house specification has been provided along with a batch of butyl dioxitol which complies with the specification.

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. The tests on the product include those for identification and assay of the active, identification of impurities, appearance and microbial purity.

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 have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. A retest period of 2 years is justified.

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. Twelve months data has been provided for three batches of the product stored at 25ºC and 40ºC. A shelf life of 2 years has been established.

H. Genetically Modified Organisms
Not applicable.

J. Other Information
Shelf life of the finished product as packaged for sale is 2 years.
Do not store above 25ºC.
Store in tightly closed original container in a dry place.
Protect from light.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies
As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended, and bioequivalence with the reference product can be assumed the results of pharmacological studies are not required.

Toxicological Studies
As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended, and bioequivalence with the reference product can be assumed the results of toxicological studies are not required.

User Safety
The applicant has provided a user safety assessment in compliance with the relevant guideline which shows permethrin is considered to be of low mammalian toxicity. The risk of exposure to the product is low due to the integral dosing device which limits the volume of the product handled at any one time to 10 ml.

Warnings and precautions as listed on the product literature are the same as those listed on the reference product and are adequate to ensure safety to users of the product:

- The product may cause neurotoxic effects and skin and eye irritation.
- Personal protective equipment consisting of protective clothing, boots and chemically resistant gloves such as rubber, PVC or nitrile should be worn when handling the veterinary medicinal product. In case of accidental spillage onto skin or into eyes rinse immediately with water.
- Wash hands after use.
- Use in a well ventilated area.
- Ensure that the treated area is dry before allowing skin contact with the treated animal.
- In case of accidental exposure seek medical advice and show the package leaflet or the label to the physician.
- Keep away from food, drink and animal feeding stuffs.

Ecotoxicity
The applicant provided a Phase I environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the product will be used on individual animals and therefore is not expected to pose a risk to the environment.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed:

- Dangerous to fish and other aquatic life. Do not contaminate ponds, waterways or ditches with the product or used container.

III.B Residues documentation

Residue
No residue studies were submitted for this application so no withdrawal period can be established. The SPC and product literature contain the necessary warnings listed under withdrawal period.

Withdrawal Periods
Not to be used in horses intended for human consumption.
Treated horses may never be slaughtered for human consumption.

The horse must have been declared as not intended for human consumption under the national horse passport legislation.

IV. CLINICAL ASSESSMENT

IV.A Pre-Clinical Studies

Pharmacology
As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended, and bioequivalence with the reference product can be assumed the results of pharmacological studies is not required.

Tolerance in the Target Species of Animals
As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended, and bioequivalence with the reference product can be assumed the results of tolerance studies is not required.

Resistance
As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended, and bioequivalence with the reference product can be assumed there is no additional risk of resistance associated with this generic product.

IV.B Clinical Studies

Laboratory Trials
As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended, and bioequivalence with the reference product can be assumed the results of clinical studies is not required.

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 benefit/risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.