Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

API-Bioxal 44.2 mg/ml Bee-Hive Solution

Date Created: August 2023

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	API-Bioxal 44.2 mg/ml Bee-Hive Solution, Bee-hive solution
Applicant	Chemicals Laif S.P.A, Viale dell'Artigianato 13, Vigonza (PD), 35010, Italy
Active substance	Oxalic Acid Dihydrate
ATC Vetcode	QP53AG03
Target species	Honey bees
Indication for use	Treatment of varroosis caused by Varroa destructor in honey bees (*Apis mellifera*).

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Full application submitted in accordance with Article 12(3) of Directive 2001/82/EC as amended.
Date of conclusion of the procedure	12/07/2023

I. SCIENTIFIC OVERVIEW

The quality / safety / efficacy aspects of this product are identical to API-Bioxal 886mg/g powder.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains Oxalic Acid Dihydrate and the excipients Glycerol and Purified Water.

The container/closure system consists of high density polyethylene (HDPE) cans. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the absence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of weighing, dissolution, filtration and filling.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is Oxalic Acid Dihydrate, an established active substance described in the inhouse monographs. 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 excipients are described in Ph. Eur.

The packaging also complies with relevant specifications.

II.C.4. Substances of Biological Origin

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.E. 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. Control tests on the finished product are those for: appearance, identification of the active, pH, density, volume, titre of the active, titre of the excipients and microbiological controls.

II.F. 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.

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.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening the immediate packaging: 12 months

Do not refrigerate or freeze.
Store in the original package.
Keep the container tightly closed in order to protect from moisture.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

Bibliographical data has been provided which show that oxalic acid is highly effective against phoretic varroa mites. Studies on the mode of action of oxalic acid have indicated that its low pH is a major contributor to the acaricidal effect. Oxalic acid has been shown to concentrate on mite legs and the edges of the exoskeleton, but none was detected in the alimentary system of mites. Therefore, mites are thought to receive the acid by contact.

The applicant has also provided bibliographical data which show that oxalic acid, the active ingredient of the product, is a natural honey constituent and its concentration in honey depends on the botanical source. No increase of oxalic acid residues over the natural content of honey is to be expected as a consequence of proper product administration. After product treatments, oxalic acid distributes into the intestine and haemolymph of honeybees where its concentration rises temporarily.

Bioequivalence was conducted against API-Bioxal powder and bioequivalence was established.

Toxicological Studies

No toxicology studies were conducted as bioequivalence was established with the reference product.

User Safety

A user risk assessment was provided in compliance with the relevant guideline.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

- This product is a highly acidic solution that may cause severe irritation to the skin and eyes. Avoid contact with the skin, eyes and mucous membranes. When handling the product wear protective clothing, chemical-resistant gloves, and safety glasses. After application, wash hands with soap and water and thoroughly wash any clothing that comes into contact with the product. In case of accidental spillage onto the skin,

wash the affected areas immediately with running water. In case of accidental eye contacts, flush the eyes immediately with clear running water for 10 minutes.

- Accidental ingestion may cause severe adverse reactions. Children should not come into contact with this veterinary medicinal product. In case of accidental ingestion, clean mouth with water and drink plenty of water or milk. Do not induce vomiting. Seek medical advice immediately.
- Do not eat, drink or smoke while handling the product

Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

Oxalate is a natural substance, use of which is not expected to alter the concentration or the distribution of the substance into the environment. A Phase II ERA was not required.

Withdrawal Periods

Based on the data provided, a withdrawal period of zero days is justified.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Tolerance in the Target Species

Tolerance studies were not required.

IV.II. Clinical Documentation

No clinical documentation was provided as bioequivalence was established with the reference product.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that the benefit/risk profile of the product is favourable.

MODULE 4

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 Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)