Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

API-Bioxal, 886 mg/g powder for in-hive use

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:
Oxalic acid dehydrate 886 mg (equivalent to 632.70 mg of Oxalic acid)

Excipients:
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Powder for in-hive use.
White fine powder.

4 CLINICAL PARTICULARS

4.1 Target Species

Honey bees *(Apis mellifera*)

4.2 Indications for use, specifying the target species

Treatment of varroosis caused by *Varroa destructor* in honey bees (*Apis mellifera*).

4.3 Contraindications

None

4.4 Special warnings for each target species

For greatest efficacy, the product should only be used when the quantity of brood in the colony is non-existent or at its lowest levels. Oxalic acid does not penetrate wax so will not kill mites within capped brood and therefore the presence of brood may noticeably reduce the efficacy of the product. As such, the product should be used in winter or following manipulation of the colony to produce a broodless state in summer (e.g. by queen caging). With regard to summer treatments following queen caging, highest levels of efficacy were achieved when a caging period of at least 25 days was used, at which point the colonies were completely broodless. Despite proper treatment, seriously damaged colonies may not survive due to the effects of varroa infestation.

Integrated Pest Management Programme
The efficacy may vary between colonies due to the conditions of use (residue presence of brood, temperature, reinfestations etc.). The product should therefore be used as a treatment amongst others within an Integrated Pest Management program, and mite drop regularly monitored.

4.5 Special precautions for use

Special precautions for use in animals
Administer the treatment without supers. All colonies in the same apiary should be treated simultaneously to avoid reinfestations. Avoid disturbance to the hives during the days after the treatment. Use of the sublimation method of administration is not recommended in summer.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

- The product may be irritant to the skin, eyes and respiratory tract, or cause contact dermatitis. Avoid direct contact and inhalation of the product.
- When handling the powder (both during vaporisation and pre-treatment phases) wear a protective mask conforming to European standard EN149 (type FFP2), gloves and protective glasses
- After application, wash hands and any skin that comes into contact with the product with soap and water. Thoroughly wash any clothing that comes into contact with the product.
- In case of eye contact, wash the eyes thoroughly with large amounts of clean running water and seek medical advice.
- Do not inhale.
- In case of accidental inhalation, breathe fresh air.
- If you have difficulty breathing, seek medical advice and show the physician this warning.
- In case of ingestion, do not induce vomiting, but seek medical advice and show the physician this warning.
- Do not eat, drink or smoke while handling the product.

4.6 Adverse reactions (frequency and seriousness)

Slightly agitation was very commonly observed during treatment with the product.
Increased adult bee mortality was very commonly observed after treatment with the product.

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

4.7 Use during pregnancy, lactation or lay

Not applicable

4.8 Interaction with other medicinal products and other forms of interactions

Do not use simultaneously with other acaricides.

4.9 Amounts to be administered and administration route

In-hive use, the product must be used as follows:

A) Posology and method of administration by trickling:
The dosage required is 5 ml per seam (gap between top bars of frames) of bees. Maximal dose is 50 ml per hive. Up to two treatments per year (winter and/or spring-summer season in brood-free colonies).

The treatment should be made in a single administration. The product should be administered using a syringe along the length of each seam of bees.

To prepare the solution, open the sachet wearing proper protective mask, gloves and glasses. Pour all the powder in the indicated amount of syrup (water and sucrose in a 1:1 ratio) and mix until dissolution. Concentration of the solution: 4,2% w/v oxalic acid in 60% w/v sucrose syrup (i.e. one bag of 35 g in 500 ml sucrose syrup that is constituted with 308 ml of water and 308 g of sucrose)".
- sachet 35g: dissolve in 500 ml of syrup (treatment for around 10 beehives).
- sachet 175g: dissolve in 2.5 l of syrup (treatment for around 50 beehives).
- sachet 350g: dissolve in 5.0 l of syrup (treatment for around 100 beehives).

B) Posology and method of administration by vaporisation
Dose is 2.3g per hive as a single administration. Maximal dose 2.3g per hive as a single administration. One treatment per year.

Use an electric resistance device for vaporisation. It is recommended to follow manufacturer's instructions in order to achieve

maximum sublimation.

Fill the pan of the vaporizer with 2.3 g of the product. Place the appliance through the entrance of the hive under the bees, avoiding contact with the honey combs. Seal the entrance of the hive to avoid escape of the bees and smoke. Turn on the vaporizer following the manufacturer's instructions for about 3 minutes and keep the hive shut for another 15 minutes. Cool down and clean the vaporizer after use to remove possible residue (max 6%, around 0.140 g). Use drinkable water for cooling and/or cleaning.

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

Significantly higher bee mortality was observed in hives that received double (by sublimation) or triple (by trickling) dosages of product. In addition, when overdosed, the over-wintering capacity of colonies was diminished and there may be detrimental effects on colony development in the future.

4.11 Withdrawal period(s)

Honey: Zero days.
Do not treat hives with super in position or during honey flow.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutical group: Ectoparasiticides for topical use, Incl. insecticides, organic acids, oxalic acid
ATCvet Code QP53AG03

5.1 Pharmacodynamic properties

Oxalic acid is an Organic acid. 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.

5.2 Pharmacokinetic particulars

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.
When 4.2% oxalic acid (in 60% sucrose syrup) was administered by trickling, peak contamination of worker bees occurred within 4 days post-treatment, declining to 9% and 2% of the maximum value at 7 and 11 days post-treatment, respectively. Oxalic acid was detected in the alimentary system and haemolymph of bees. Administration of oxalic acid by sublimation resulted in lower intestinal levels and a faster decline of total levels compared to trickling.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silica, colloidal hydrate
Glucose monohydrate

6.2 Major incompatibilities

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

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the immediate packaging: 3 months.
Shelf-life after reconstitution according to directions: 24 hours

6.4 Special precautions for storage

Do not refrigerate or freeze.
Store in the original package.
Keep the original package tightly closed in order to protect from light and moisture.
Store away from foodstuffs.

6.5 Nature and composition of immediate packaging

Multilayer polyester-Aluminium-Polyethylene laminated bags, heat sealed, containing 35 g, 175 g and 350 g of powder.
Pack sizes:
1 x 35 g of powder
1 x 175 g of powder
1 x 350 g of powder
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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.

API-Bioxal should not be allowed to contaminate water courses as this may be dangerous for fish and other aquatic organisms.

7 MARKETING AUTHORISATION HOLDER

Chemicals Laif S.P.A
Viale dell'Artigianato 13 - Vigonza (PD)
35010
Italy

8 MARKETING AUTHORISATION NUMBER(S)

VPA10388/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 07 April 2017
Date of last renewal: 30 April 2021

10 DATE OF REVISION OF THE TEXT

June 2021