[Version 9.1,11/2024]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Api-Bioxal 0.71 g/g bee-hive powder

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substances:
0.71 g oxalic acid equivalent to 0.995 g of oxalic acid dihydrate

Excipients:

Qualitative composition of excipients and other constituents
Silica colloidal hydrated

White fine powder.

3. CLINICAL INFORMATION

3.1 Target species

Honey bees (*Apis mellifera*)

3.2 Indications for use for each target species

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

3.3 Contraindications

None.

3.4 Special warnings

For greatest efficacy, the veterinary medicinal 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 veterinary medicinal product. As such, the veterinary medicinal 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 veterinary medicinal product should therefore be used as a treatment amongst others within an Integrated Pest Management program, and mite drop regularly monitored.

3.5 Special precautions for use

Special precautions for safe use in the target species:

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 veterinary medicinal product may be irritant to the skin, eyes and respiratory tract, or cause contact dermatitis. Avoid contact with the skin, eyes, mucous membranes and inhalation -.
Personal protective equipment consisting of protective mask conforming to European standard EN149 (type FFP2), protective gloves and protective glasses should be worn when handling the veterinary medicinal product (both during vaporisation and pre-treatment phases). After application, wash hands and any skin that comes into contact with the veterinary medicinal product with soap and water. Thoroughly wash any clothing that comes into contact with the veterinary medicinal 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 veterinary medicinal product.

Special precautions for the protection of the environment:

The veterinary medicinal product should not enter water courses as oxalic acid may be dangerous for fish and other aquatic organisms.

3.6 Adverse events

Honey bees:

Very common (>1 colony/ 10 colonies treated):	Bee systemic disorder [1;2;]

[1] Slight agitation of colony during treatment
[2] Increased adult bee mortality rate after treatment

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the immediate packaging for respective contact details.

3.7 Use during pregnancy, lactation or lay

Not applicable.

3.8 Interaction with other medicinal products and other forms of interaction

Do not use simultaneously with other acaricides.

3.9 Administration routes and dosage

In-hive use, the veterinary medicinal 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) occupied by 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 veterinary medicinal product should be administered using a syringe along the length of each seam of bees.

To prepare the solution, open the bag 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: 4,4% w/v oxalic acid in 60% w/v sucrose syrup (i.e. one bag of 31 g in 500 ml sucrose syrup that is constituted with 308 ml of water and 308 g of sucrose)".
- bag 31 g: dissolve in 500 ml of syrup (treatment for around 10 beehives).
- bag 156 g: dissolve in 2.5 l of syrup (treatment for around 50 beehives).
- bag 312 g: dissolve in 5.0 l of syrup (treatment for around 100 beehives).

B) Posology and method of administration by vaporisation
Dose is 2 g per hive as a single administration. Maximal dose 2 g 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 g of the veterinary medicinal product, following the manufacturer's instructions. Keep the hive shut after the treatment for 15 minutesto avoid escape of the bees and smoke. Use drinkable water for cooling and/or cleaning.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Significantly higher bee mortality was observed in hives that received double (by sublimation) or triple (by trickling) dosages of veterinary medicinal 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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Honey: zero days.
Do not use in colonies with supers or during honey flow.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code : QP53AG03.

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

Oxalic acid, the active ingredient of the veterinary medicinal 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 veterinary medicinal product administration. After veterinary medicinal product treatments, oxalic acid distributes into the intestine and haemolymph of honeybees where its concentration rises temporarily.
When 4.4% 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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 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.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Multilayer polyester-Aluminium-Polyethylene laminated bags, heat sealed, containing 31 g, 156 g and 312 g of powder.

Pack sizes:
1 x 31 g of powder
1 x 156 g of powder
1 x 312 g of powder

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.
The veterinary medicinal product should not enter water courses as oxalic acid may be dangerous for fish and other aquatic organisms.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

CHEMICALS LAIF S.P.A.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 24/06/2011

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

MM/YYYY

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product not subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE - COMBINED LABEL AND PACKAGE LEAFLET

Multilayer polyester-Aluminium-Polyethylene laminated bags

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Api-Bioxal 0.71 g/g bee-hive powder

2. COMPOSITION

Each g contains:
Active substance:
0.71 g oxalic acid equivalent to 0.995 g of oxalic acid dihydrate
Excipients:
Silica colloidal hydrated.

White fine powder.

3. PACKAGE SIZE

31 g
156 g
312 g

4. TARGET SPECIES

Honey bees (*Apis mellifera*)

5. INDICATIONS FOR USE

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

6. CONTRAINDICATIONS

Contraindications
None

7. SPECIAL WARNINGS

Special warnings

For greatest efficacy, the veterinary medicinal 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 veterinary medicinal product. As such, the veterinary medicinal 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.

Special precautions for safe use in the target species:
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 veterinary medicinal product may be irritant to the skin, eyes and respiratory tract, or cause contact dermatitis. Avoid contact with the skin, eyes, mucous membranes and inhalation.
Personal protective equipment consisting of protective mask conforming to European standard EN149 (type FFP2), protective gloves and protective glasses should be worn when handling the veterinary medicinal product (both during vaporisation and pre-treatment phases).After application, wash hands and any skin that comes into contact with the veterinary medicinal product with soap and water. Thoroughly wash any clothing that comes into contact with the veterinary medicinal 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 veterinary medicinal product.

Special precautions for the protection of the environment:
The veterinary medicinal product should not enter water courses as oxalic acid may be dangerous for fish and other aquatic organisms.

Interactions with other medicinal products and other forms of interaction:
Do not use simultaneously with other acaricides.

Overdose:
Significantly higher bee mortality was observed in hives that received double (by sublimation) or triple (by trickling) dosages of veterinary medicinal 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.

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

8. ADVERSE EVENTS

Adverse events

Honey bees:

Very common (>1 colony/ 10 colonies treated):	Bee systemic disorder (Slight agitation of colony during treatment; Increased adult bee mortality rate after treatment)

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed on this label, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also

report any adverse events to the marketing authorisation holder or its local representative using the contact details on this label, or via your national reporting system.

9. DOSAGE FOR EACH TARGET SPECIES, ROUTES AND METHOD OF ADMINISTRATION

Dosage for each species, routes and method of administration

In-hive use, the veterinary medicinal 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) occupied by 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 veterinary medicinal product should be administered using a syringe along the length of each seam of bees. To prepare the solution, open the bag 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: 4,4% w/v oxalic acid in 60% w/v sucrose syrup (i.e. one bag of 31 g in 500 ml sucrose syrup that is constituted with 308 ml of water and 308 g of sucrose)".
- Bag31 g: dissolve in 500 ml of syrup (treatment for around 10 beehives).
- Bag 156 g: dissolve in 2.5 l of syrup (treatment for around 50 beehives).
- Bag 312 g: dissolve in 5.0 l of syrup (treatment for around 100 beehives).

B) Posology and method of administration by vaporization:
Dose is 2 g per hive as a single administration. Maximal dose 2 g 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 g of the veterinary medicinal product, following the manufacturer's instructions. Keep the hive shut after the treatment for 15 minutes to avoid escape of the bees and smoke. Use drinkable water for cooling and/or cleaning.

10. ADVICE ON CORRECT ADMINISTRATION

Advice on correct administration

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

11. WITHDRAWAL PERIODS

Withdrawal periods
Honey: zero days.
Do not use in colonies with supers or during honey flow.

12. SPECIAL STORAGE PRECAUTIONS

Special storage precautions
Keep out of the sight and reach of children.
Do not refrigerate or freeze. Store in the original package. Keep the container tightly closed in order to protect from light and moisture. Store away from foodstuffs.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.

13. SPECIAL PRECAUTIONS FOR DISPOSAL

Special precautions for disposal
Medicines should not be disposed of via wastewater or household waste. This veterinary medicinal product should not enter water courses as oxalic acid may be dangerous for fish and other aquatic organisms. Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment. Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

14. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Classification of veterinary medicinal products
Veterinary medicinal product not subject to prescription.

15. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

Marketing Authorisation Number:

Pack sizes
1 x 31 g of powder
1 x 156 g of powder
1 x 312 g of powder
Not all pack sizes may be marketed.

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised

{MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

17. CONTACT DETAILS

Contact details

Marketing authorisation holder and contact details to report suspected adverse events:
CHEMICALS LAIF S.p.A.
Viale dell'Artigianato 13,
35010 Vigonza (PD), Italy.
qppv@chemicalslaif.it
info@chemicalslaif.it
+39 (049)626281
+39 3880593724

Manufacturer responsible for batch release:

CHEMIFARMA S.p.A.,
Via Don Eugenio Servadei 16,
47122 Forlì (FC), Italy.

Local representatives and contact details to report suspected adverse events: *To be completed nationally.*

18. OTHER INFORMATION

19. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

20. EXPIRY DATE

Exp {mm/yyyy}

Shelf life after first opening the container: 3 months.
Shelf life after reconstitution according to directions: 24 hours.

21. BATCH NUMBER

Lot {number}