[Version 9.1,11/2024]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apifor 600 mg/g bee-hive solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Active substance:
600 mg formic acid

Excipient:

Qualitative composition of excipients and other constituents
Purified water

Clear colourless liquid.

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

Do not use at daily temperatures outside the specified range (10-30°C)

3.4 Special warnings

Use according to local treatment recommendations, if available.
Colonies require adequate ventilation during treatment.
All colonies in the same apiary should be treated simultaneously to avoid robbing.
The veterinary medicinal product should only be used as part of an Integrated Varroa Management program.
It is highly recommended to monitor phoretic mite levels monthly during periods of brood rearing and treat when local thresholds are reached.
To ensure sufficient efficacy the veterinary medicinal product should be used when outdoor temperatures exceed 10°C.

Integrated Pest Management Programme
The efficacy may vary between colonies due to the conditions of use (environmental factors related to the site and climatic conditions, temperature, genetics and level of infestation, reinfestation, numbers of bees, strength of the colony, size of the brood, bee mortality etc.). The veterinary medicinal product should therefore be used as a treatment amongst others within an Integrated Varroa Management program, and mite drop should be regularly monitored.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Do not treat with honey supers. Do not disturb the hives for minimum 10 days during the treatment.

Temperatures: to ensure a good efficacy of the veterinary medicinal product the ideal range of external temperatures during the treatment should be 10-30°C. Temperatures above 30°C during the early three days of treatment may cause excessive brood mortality and queen loss. Treatment should be postponed until temperatures drop. Colonies require adequate access to fresh air during the treatment. The hive entrance needs to be fully open all through the treatment (min. 10 days). Entrance reducers must be removed to prevent damage to colonies. To avoid an intolerable formic acid concentration, it is essential to ensure sufficient ventilation over the entire treatment period. Do not destroy queen cells that may be observed prior to or after the treatment. Supercedure, even if thought to be set in motion by treatment, is a natural process, and should be allowed to proceed for the health of the colony. Verify the colony is queen-right one month after treatment. Mother and daughter queens present post treatment are not uncommon. Bearding behavior may be observed. Colonies should have good food reserves at time of treatment, should not be fed during treatment. Check the food reserves after the end of treatment and if needed add food.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
The veterinary medicinal product is a clear colourless liquid, very volatile, strongly corrosive, with a pungent smell. Formic acid may cause hypersensitivity (allergy). People with known hypersensitivity to formic acid should avoid contact with the veterinary medicinal product. This veterinary medicinal product is irritating to the skin, eyes and the respiratory tract. Avoid contact with the skin, eyes and mucous membranes and inhalation of vapours.
Personal protective equipment consisting of protective clothing (EN 14605), chemical resistant gloves (EN 374), safety goggles (EN 166) and mask with a filter (EN 14387) should be worn when handling the veterinary medicinal product. Remove heavily contaminated clothes as soon as possible and wash before re-use. In case of accidental spillage onto skin, wash the affected areas immediately with running water, seek medical advice immediately and show the package leaflet or the label to the physician. In case of accidental spillage into the eyes, rinse immediately with clear running water for 10 minutes, seek medical advice immediately and show the package leaflet or the label to the physician.
In case of accidental inhalation move to fresh air. If irritation persists after any type of exposure, seek medical advice and show the package leaflet or the label to the physician.
Keep children well away during the application of the veterinary medicinal product. In case of accidental ingestion immediately rinse mouth and drink plenty of water, but DO NOT induce vomiting, seek medical advice immediately and show the package leaflet or the label to the physician.
Do not eat, drink or smoke whilst handling and applying the veterinary medicinal product.
Wash hands with soap and water directly after use.

Special precautions for the protection of the environment:
Not applicable.

Other precautions:
This product is corrosive. Avoid contact with metal surfaces.

3.6 Adverse events

Honey bees:

Very rare (<1 colony / 10 000 colonies treated, including isolated reports):	Bee systemic disorder [1;2]; Queen bee rejection; Bee brood mortality

[1] Disturb colony activity
[2] Increased adult bee mortality rates 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 product must be used as follows:
Recommended dosage for beehive volume: 2.0 – 2.5 g formic acid per litre beehive volume, equal to 3.8-4.8 mL of product/L of beehive volume. The recommended dose must be adjusted to the volume of the beehive used. For example for Dadant hive (about 60 L up to 90 L of volume with the supper) the total dosage to be used is 228-288 ml per beehive (342-432 ml per beehive with supper).

The total amount of veterinary medicinal product per hive should be adjusted depending on the level of infestation, the colony strength and the external conditions (temperature and humidity).

Method and duration of treatment: the veterinary medicinal product is introduced into the beehive with the aid of suitable dispensers (evaporators). The particularity of this application consists in the continuous and constant evaporation of small doses per unit time over a prolonged period. The evaporation of the formic acid into the colony must occur with the maximum possible regularity for a minimum period of 10 days until complete evaporation of the product. The dispenser is removed when no more formic acid is present in the reservoir/container. It is recommended to use suitable applicators/evaporators which must be placed in the upper part of the volume of the beehive, in order to ensure a better diffusion of the vapours and that are specifically developed for formic acid evaporation with a wick and a patented evaporation system that allows a slow release of the acid solution (*e.g.* B.L.V. Formic, Nassenheider Professional).
To use horizontal dispensers, it is necessary to place empty honey supers on the colonies. This results in increased volume and dosage of the hive.

Hive type / Volume (L) per single box	
Langstroth (one body) / 44L	Dadant / 60L
Lusitana and Reversível / 54L	AZ hive / 76L

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

In case of overdose extract the evaporator and reduce the surface of evaporation. The use of higher dose than recommended could lead to excessive brood loss, adult bee mortality, queen loss, and/or absconding. In case of overdose, increase hive ventilation by creating additional entrances from top to bottom. Check the presence of queen 2 weeks after application.

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 during the honey flow.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code : QP53AG01

4.2 Pharmacodynamics

Formic acid from the product acts by fumigation, or vapour action.
Formic acid is active against mites on adult bees and is known to kill mites and their offspring within capped brood cells.
The mode of action of formic acid has not been fully elucidated. The available data show an inhibition of the mitochondrial respiratory chain and acidosis of body tissues. *Varroa destructor* is more susceptible for this mechanism than the bee, this explains the therapeutic selectivity.

4.3 Pharmacokinetics

The pharmacokinetics of formic acid in honeybees has not been studied.

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: 4 years.
Shelf life after first opening the immediate packaging: 3 months.

5.3 Special precautions for storage

Protect from direct sunlight.
Store in a dry place.
Store in the original container.
Keep the container tightly closed in a well-ventilated area, away from sulphuric acid, strong oxidizing agents (e.g. nitric acid, peroxides, perchlorates, chlorites) and sources of ignition.

5.4 Nature and composition of immediate packaging

High density polyethylene (HDPE) bottle and container opaque white with High density polyethylene screw cap.
Pack sizes:
1 x 1L Bottle
1 x 5L Container
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 formic 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: {DD/MM/YYYY}

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 – <u>COMBINED LABEL AND PACKAGE LEAFLET</u>

{HDPE / Bottle – HDPE / Container}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apifor 600 mg/g bee-hive solution

2. COMPOSITION

Each gram contains:
Active substance:
600 mg formic acid
Excipient:
Purified water
Clear colourless liquid.

3. PACKAGE SIZE

1L
5L

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
Do not use at daily temperatures outside the specified range (10-30°C)

7. SPECIAL WARNINGS

Special warnings

<u>Special warnings:</u>
Use according to local treatment recommendations, if available.
Colonies require adequate ventilation during treatment.
All colonies in the same apiary should be treated simultaneously to avoid robbing.

The veterinary medicinal product should only be used as part of an Integrated Varroa Management program.
It is highly recommended to monitor phoretic mite levels monthly during periods of brood rearing and treat when local thresholds are reached.
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Special precautions to be taken by the person administering the veterinary medicinal product to animals:

The veterinary medicinal product is a clear colourless liquid, very volatile, strongly corrosive, with a pungent smell. Formic acid may cause hypersensitivity (allergy). People with known hypersensitivity to formic acid should avoid contact with the veterinary medicinal product.
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Keep children well away during the application of the product. In case of accidental ingestion immediately rinse mouth and drink plenty of water, but DO NOT induce vomiting, seek medical advice immediately and show the package leaflet or the label to the physician.
Do not eat, drink or smoke whilst handling and applying the veterinary medicinal product.
Wash hands with soap and water directly after use.

Special precautions for the protection of the environment:
Not applicable.

Other precautions:
This veterinary medicinal product is corrosive. Avoid contact with metal surfaces.

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

Overdose:

In case of overdose extract the evaporator and reduce the surface of evaporation. The use of higher dose than recommended could lead to excessive brood loss, adult bee mortality, queen loss, and/or absconding. In case of overdose, increase hive ventilation by creating additional entrances from top to bottom. Check the presence of queen 2 weeks after application.

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 rare (<1 colony / 10 000 colonies treated, including isolated reports):	Bee systemic disorder (Disturb colony activity; increased adult bee mortality rate after treatment); Queen bee rejection; Bee brood mortality

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: {national system details}

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

Dosage for each species, routes and method of administration
In hive use, the product must be used as follows:
Recommended dosage for beehive volume: 2.0 - 2.5 g formic acid per litre beehive volume, equal to 3.8-4.8 mL of product/L of beehive volume. The recommended dose must be adjusted to the volume of the beehive used. For example for Dadant hive (about 60 L up to 90 L of volume with the supper) the total dosage to be used is 228-288 ml per beehive (342-432 ml per beehive with supper).
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To use horizontal dispensers, it is necessary to place empty honey supers on the colonies. This results in increased volume and dosage of the hive.

Hive type / Volume (L) per single box	
Langstroth (one body) / 44L	Dadant / 60L
Lusitana and Reversível / 54L	AZ hive / 76L

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 (environmental factors related to the site and climatic conditions, temperature, genetics and level of infestation, reinfestation, numbers of bees, strength of the colony, size of the brood, bee mortality etc.). The veterinary medicinal product should therefore be used as a treatment amongst others within an Integrated Varroa Management program, and mite drop should be regularly monitored.

11. WITHDRAWAL PERIODS

Withdrawal periods

Honey: Zero days

Do not use during the honey flow.

12. SPECIAL STORAGE PRECAUTIONS

Special storage precautions

Keep out of the sight and reach of children.

Protect from direct sunlight.

Store in a dry place.

Store in the original container.

Keep the container tightly closed in a well-ventilated area, away from sulphuric acid, strong oxidizing agents (e.g. nitric acid, peroxides, perchlorates, chlorites) and sources of ignition.

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 formic 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

EU/0/00/000/000

Pack sizes

1 x 1L

1 x 5L
Not all pack sizes may be marketed.

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised

{DD/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 manufacturer responsible for batch release and contact details to report suspected adverse events:
CHEMICALS LAIF S.P.A.
Viale dell'Artigianato 13
35010 Vigonza (PD), Italy
{telephone number}
{E-mail address}

Local representatives and contact details to report suspected adverse reactions: {applicable to PT, SI}

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 packaging: 3 months

21. BATCH NUMBER

Lot {number}