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AGENCE NATIONALE DU
MEDICAMENT VETERINAIRE

FRENCH AGENCY FOR FOOD, ENVIRONNEMENTAL AND OCCUPATIONAL HEALTH SAFETY

FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

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PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Optivar 500 mg bee-hive strips for honey bees

06 May 2026

PRODUCT SUMMARY

EU procedure number	FR/V/0515/001/DC
Name, strength and pharmaceutical form	Optivar 500 mg bee-hive strips for honey bees
Applicant	Veto-Pharma 12-14 Rue De La Croix Martre 91120 Palaiseau, France
Active substance(s)	Amitraz
ATC vetcode	QP53AD01
Target species	Honey bee (*Apis mellifera)*
Indication for use	Treatment of varroosis due to *Varroa destr*uctor sensitive to amitraz. In-hive use. Each strip contains 500mg of amitraz. Use two strips per brood chamber.

Optivar 500 mg bee-hive strips for honey bees	FR/V/0515/001/DC
VETO-PHARMA	DCP
Publicly available assessment report	

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Article 22 – Bibliographic application (Regulation (EU) 2019/6)
Date of completion of the original decentralised procedure	01 April 2026
Concerned Member States for original procedure	BG, CY, CZ, EE, ES, EL, FR, HR, HU, IE, IT, LT, LV, PL, PT, RO, SI, UK(NI)

*Please be aware that certain parts of the dossier may be varied and consequently be subject to protection of technical documentation – for these and other changes of referenceability to parts of the dossier, please see chapter POST-AUTHORISATION PROCEDURES

1. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.

It has been shown that the VMP can be safely used in the target species; the reactions observed are indicated in the SPC.

The VMP is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.

The efficacy of the VMP was demonstrated according to the claims made in the SPC.

The overall risk/benefit analysis is in favour of granting a marketing authorisation.

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

A. Product description

The VMP contains amitraz as active substance (0.5 g / strip) and the excipients calcium oxide, erucamide and ethylene vinyl acetate.

The container closure system consists of a heat-sealed, multi-layer sachet.

The choice of the formulation is justified.

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

B. Description of the manufacturing method

The VMP is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

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

C. Production and control of starting materials

The active substance is amitraz, an established active substance described in the British Veterinary Pharmacopeia. 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.

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

D. Control tests carried out on isolated intermediates during the manufacturing process

Not applicable.

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 VMP.

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.

F. Stability tests

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 VMP throughout its shelf life when stored under the approved conditions.

The in-use shelf life of the opened VMP is supported by the data provided. The recommendations in the product leaflet should be followed.

G. Other information

Not applicable.

3. SAFETY DOCUMENTATION (safety and residues tests)

A. Safety tests

Pharmacological studies

See part 4.A.

Toxicological studies

The toxicological profile of amitraz was assessed by the CVMP, JMPR and EPA and the applicant has provided bibliographical data and conducted an oral extended one-generation reproduction study in rats.

The acute toxicity of amitraz and its metabolites is moderate to low in laboratory species.

Repeated dose toxicity studies in laboratory species showed that the dog was the most sensitive species.

In all cases, the principal sign of toxicity was central nervous system (CNS) depression.

In oral reproduction studies with rats, mice and rabbits, amitraz interacted with sexual hormone storage and led to a longer cycle length, prolonged estrus, diestrus and proestrus periods and had adverse effects in fertility of male mice.

In the GLP oral extended one-generation toxicity study in rats conducted by the applicant, no effects on reproductive performance and no neurological signs were shown in F0 and F1 generations up to the highest tested dose of 7.5 mg/kg.

Amitraz and its metabolites did not show any genotoxic potential.

Bibliographic carcinogenic data with amitraz showed an increase in incidence of lymphoreticular tumours or of hepatocellular carcinoma in female mice only.

No carcinogenicity was reported when rats received orally 10-13 mg amitraz/kg/day for 2 years. Hence, the increased incidence of hepatocellular and lymphoreticular tumours in female mice was not considered to be significant to human health.

Other studies

In two *in vivo* GLP studies, the VMP was not irritating for both rabbit's skin and rat's skin.

Eye irritation of amitraz was documented from bibliographic references.

In an *in vivo* GLP study in guinea pig, the VMP was not a skin sensitizer.

Neurotoxicity data showed that amitraz decreased the motor activity at low doses (1 mg/kg) and affected the visual evoked potential at intermediate (50 mg/kg) and high doses in rats.

In the published literature, decrease of the plaque forming cell in the spleen was observed at 26.5 mg/kg. This observation should be considered to be less meaningful because of other toxicities at lower exposure concentrations.

Observations in humans

Amitraz is not used as human medicine. However, the applicant has provided bibliographical data on pharmacological/pharmacokinetic in humans. Main adverse effects after ingestion are transient and reversible and consisted principally in moderate to severe CNS depression. An ADI of 0.003 mg/kg (180 µg/person) was established by EMA. This is similar to the ADI determined by JMPR.

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that, considering the low margins of exposure, a risk exists in the case of oral ingestion or ocular contact. However, warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH topic GL6. According to the respective decision tree the assessment can stop in Phase I.
As mentioned on the product literature, the veterinary medicinal product should not enter water courses as amitraz may be dangerous for fish and other aquatic organisms.

B. Residues documentation

Maximum Residue Limits

The active substance, amitraz, is included in table 1 of the annex to Commission Regulation (EU) No 37/2010, as follows:

Marker residue	Animal Species	MRL	Target Tissues	Other Provisions	Therapeutic Classification
Sum of amitraz and all metabolites containing the 2,4-DMA moiety, expressed as amitraz	Bovine	200 µg/kg 200 µg/kg 200 µg/kg 10 µg/kg	Fat Liver Kidney Milk	No entry	Antiparasitic agents/ Agents against ectoparasites
	Ovine	400 µg/kg 100 µg/kg 200 µg/kg 10 µg/kg	Fat Liver Kidney Milk		
	Caprine	200 µg/kg 100 µg/kg 200 µg/kg 10 µg/kg	Fat Liver Kidney Milk		

	Porcine	400 µg/kg 200 µg/kg 200 µg/kg	Skin + fat Liver Kidney		
	Bees	200 µg/kg	Honey		

The MRL status of excipients listed in section 2 of the SPC is indicated in the following table.

Excipient	**MRL status**
Ethylene vinyl acetate copolymer	Out of scope
Calcium oxide	Table 1, for all producing species, without ADI and with no MRL required
Erucamide	Out of scope list, for in-hive use only

The composition of the candidate product OPTIVAR 500 MG BEE-HIVE STRIPS FOR HONEY BEES is acceptable according to the European Regulation (EC) No 470/2009.

Residue tests

The applicant has conducted two GLP residue depletion studies in honey bees: one study with Dadant beehives and another one with Langstroth beehives.

The honey samples were analysed using liquid-liquid extraction for sample preparation using acetonitrile and sodium hydroxide, followed by LC-MS/MS detection. Amitraz-D2 and lidocaine were used as internal standards.
Residues in wax were extracted from homogenised samples by extraction with acetonitrile and sodium hydroxide. Then the extracts were purified by dispersive SPE and quantified by a LC-MS/MS method. Amitraz-D2 and lidocaine were used as internal standards.
The methods were fully validated.

Withdrawal Periods

Based on the data provided above, a withdrawal period of zero days for honey is justified, with the following restrictions:

Do not use during honey flow.
Do not extract honey from the brood chamber.
Do not harvest honey for human consumption while the treatment is in place.
Brood combs should be replaced with new foundation at least every three years.
Do not reuse brood frames as honey frames.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

A. Pre-Clinical Studies

Pharmacology

OPTIVAR 500 MG BEE-HIVE STRIPS FOR HONEY BEES is a strip for beehive containing amitraz. This product is indicated for treatment of varroosis due to *Varroa destructor* sensitive to amitraz, with a recommended dosage regimen of 2 strips of 500 mg of amitraz per brood chamber for 6 or 10 consecutive weeks.

This application is submitted in accordance with Article 22 – Bibliographic application of Regulation (EU) 2019/6.

The applicant has provided bibliographical data to document the pharmacology of amitraz.

According to the target species, honeybees, pharmacokinetics is not relevant.

Development of resistance and related risk in animals

The applicant has provided bibliographical data on the resistance of *Varroa* against amitraz and on the mechanism of this resistance.

To reduce the risk of emergence of *Varroa* resistance to amitraz relevant warnings are included in the SPC.

Dose determination and confirmation

The applicant has provided bibliographic references that support the proposed dose of amitraz for the treatment of varroosis due to *Varroa destructor.*

As OPTIVAR corresponds in pharmaceutical form, active ingredient and proposed dose to APIVAR, the data collected for APIVAR can be bridged to the formulation of OPTIVAR.

The recommended dose of 2 strips per brood chamber can thus be accepted for OPTIVAR based on the data provided.

Tolerance in the target species of animals

The applicant has provided bibliographical data to document the tolerance in bees (adult, drone, larvae) as well for the colony.

In addition, the tolerance of OPTIVAR in bees was followed in 4 clinical studies, at the recommended dosage and in overdose in one of the trials (4 strips per brood chamber in Dadant hives, with brood for a 10 week exposure).

Transient behavioural disorders (e.g., fleeing reaction, aggressive behaviour) was very rarely observed when the strips are first placed in the hive. This is believed to be a defensive behaviour rather than an adverse reaction to the veterinary medicinal product, per se.

No adverse effects were seen following two times the recommended dose.

The product literature accurately reflects the type and incidence of adverse effects, which might be expected.

B. Clinical trials

The applicant presented bibliographic references and four field clinical trials that were conducted in accordance with the current Guideline on VMP controlling *Varroa destructor* parasitosis in bees.

Three trials have confirmed the efficacy of the candidate product in Dadant hives and/or Langstroth hives, with brood, at the recommended dose of 2 strips per brood chamber for 9/10 weeks. The percentages of efficacy were considered sufficient (above or close to 95%) at the end of the studies.

The last trial has assessed the efficacy of the candidate product in Dadant hives with brood, at the recommended dose of 2 strips per brood chamber for 6 weeks. The efficacy percentage (91%) was below 95%.

However, from results of all trials, efficacy above 95% was reached in certain bee-hives from D42 (6 weeks after application). It was concluded that the level of efficacy when the product is applied for 6 weeks is acceptable when brood levels are low at the start of treatment (approximately one brood frame, *i.e.* ≤ 10000 brood cells), and when no brood is present in the colony at 5-6 weeks after treatment initiation.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the VMP is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable and the quality and safety of the VMP for humans and the environment is acceptable.